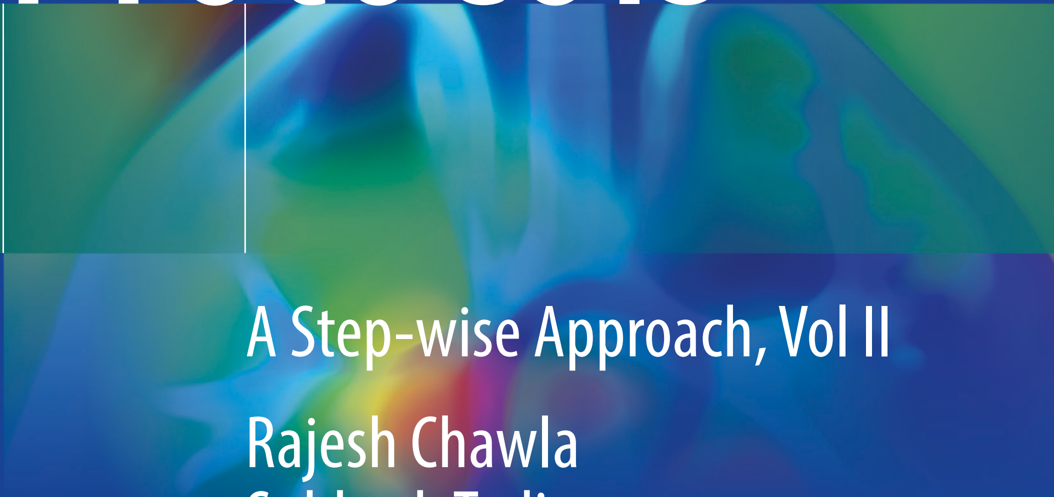
ICU Protocols



A Step-wise Approach, Vol II

Rajesh Chawla
Subhash Todi
Editors

Third Edition

ISCCM
INDIAN SOCIETY OF
CRITICAL CARE MEDICINE

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An endeavour of Indian College of Critical Care Medicine under the auspices of Indian Society of Critical Care Medicine (ISCCM).

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To my parents, my wife Renu, and my children Ankit, Aakanksha, Aakriti, Vaibhav, and especially little Reneha, for their unconditional love, encouragement, and unwavering support. A special note of gratitude to Dr. Sudha Kansal, as well as my students, residents, fellows, and colleagues, whose passion and commitment continually inspire and educate me.

—Rajesh Chawla

To my mother, my wife Shailja, my daughter Suchira, and son-in-law Krishna, for their enduring understanding, patience, and support during the creation of this manual. Your love and encouragement made this work possible.

—Subhash Todi

Preface

We are delighted to present the third edition of *ICU Protocols: A Stepwise Approach,* an official publication of the Indian Society of Critical Care Medicine (ISCCM). Since the release of the second edition in 2020, the field of critical care medicine has undergone significant advancements, necessitating a comprehensive update to this widely acclaimed manual.

This new edition remains true to its fundamental objective: to provide clinicians, residents, fellows, and allied healthcare professionals with a practical and evidence-based guide for managing critically ill patients at the bedside. To maintain clarity and usability, we have preserved the stepwise approach, rich with flowcharts, tables, bullet points, and illustrations, while expanding and updating the content to address contemporary challenges and innovations.

The third edition introduces several new chapters that reflect the evolving landscape of critical care:

- *Searching Literature for Clinical Questions*
- *Artificial Intelligence in Critical Care*
- *Safety and Error in ICU*
- *Pharmacological Principles and Drug Interactions in ICU*
- *Acute Dermatological Emergencies in ICU*
- *Pituitary, Thyroid, and Adrenal Emergencies in ICU*
- *Calcium, Phosphorus, and Magnesium Disorders*
- *Rapid Diagnostic Tools in Microbiology in ICU*
- *Severe Gram-Positive Infections in ICU*
- *Managing Severe Gram-Negative Infections in ICU*
- *Necrotizing Skin Infections in ICU*

Each of these chapters provides detailed, practical insights into the latest diagnostic and therapeutic strategies, underscored by cutting-edge research and technological advancements. For example, the chapter on *Artificial Intelligence in Critical Care* delves into AI's potential to revolutionize patient monitoring, predictive analytics, and clinical decision-making. The chapter on *Safety and Error in ICU* focuses on strategies to minimize preventable harm and enhance patient safety in the complex ICU environment.

Existing chapters from the previous editions have been extensively revised, incorporating the latest evidence-based guidelines and clinical practices. Notable updates include expanded discussions on pharmacology, drug interactions, and emerging diagnostic technologies to aid clinicians in rapidly identifying and managing critical conditions.

In addition, the appendix section has been significantly updated, including enhanced *Dosing Guidelines,* new drug formulations, and an expanded *Glossary of Statistical Terms.* These updates aim to simplify understanding of clinical data and support informed decision-making.

This edition is the result of collaboration between multidisciplinary experts, including intensivists, infectious disease specialists, endocrinologists, and microbiologists. The "Suggested Reading" sections have been enriched with references to the latest landmark studies, online resources, and current guidelines to ensure comprehensive coverage of the topics discussed.

As critical care continues to evolve, we recognize that this manual is a living document that will require future updates to reflect ongoing advancements. We hope this edition serves as an indispensable resource for improving patient outcomes and fostering excellence in critical care practices worldwide.

New Delhi, Delhi, India — Rajesh Chawla
Kolkata, West Bengal, India — Subhash Todi

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Part I

Endocrine and Metabolic System

Hyponatremia

1

Rajesh Chawla, Subhash Todi, Raju Shakya,
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Case Vignette 1
A 70 kg diabetic man presents with polyuria, serum Na 130 mEq/L, blood urea nitrogen (BUN) 18, and urine osmolality 220 mOsmol/kg. His random blood sugar (RBS) was found to be 400 mg/dL (Table 1.4).

Case Vignette 2
An 80 kg woman presents with nausea, loss of appetite, and weakness. She has no signs of dehydration. On evaluation, she has serum Na 130 mEq/L, RBS 120 mg/dL, BUN 10, urine osmolality 160 mOsmol/kg, and urine Na 45 (Table 1.5).

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Case Vignette 3

An 80 kg female case of road traffic accident with intracranial hemorrhage presents to emergency room (ER) with BP of 100/60 mmHg with high urine output. On evaluation, she has serum Na 128 mEq/L, RBS 125 mg/dL, BUN 10, urine osmolality 163 mOsm/kg, and urine Na 250. Inferior venacava (IVC) diameter is <2 cm with more than 50% collapsibility (Table 1.6).

Case Vignette 4

A 55 kg man presents with fever, abdominal cramps, vomiting, loose motion, and decreased urine output for 3 days. He has sunken eyes, a dry tongue, and poor skin turgor. On evaluation, he has S Na 128 mEq/L, RBS 120 mg/dL, BUN 10, urine osmolality 180 mOsm/kg, and urine Na 15 (Table 1.7).

Case Vignette 5

A 70 kg man presented with headache, confusion, and nausea for the past 36 h. On evaluation, serum Na is 110 mEq/L and RBS 124 mg/dL? (Table 1.8).

Case Vignette 6

A 65 kg woman was referred from another hospital with a fall in serum Na to 110 mEq/L in 24 h, although with no symptoms. Her RBS was found to be 142 mg/dL (Table 1.9).

Hyponatremia is primarily a disorder of water regulation across different fluid compartments in the body. The incidence of hyponatremia and hypernatremia in the ICU is around (15–30)%, bearing a mortality of around (30–40)% compared to patients with normal sodium levels. Hyponatremia is defined as serum sodium less than 135 mEq/L. It is considered severe if serum sodium is less than 120 mEq/L. It represents a relative excess of water to sodium. Total body sodium may be normal, low, or high.

Hyponatremia can be induced by increased water intake and/or impaired water excretion. Too rapid correction can result in neurological complications. Hyponatremia is said to be acute when it develops over less than 48 h and is called chronic hyponatremia if it has been present for more than 48 h or for an unknown duration.

Step 1: Initiate Resuscitation (Refer Chap. 24)

- The airway is to be assessed and secured first in a patient with severe hyponatremia who is not able to maintain the airway.
- Ventilatory support may be needed—noninvasive or invasive.
- Intravenous access should be secured for resuscitation with suitable fluids as necessary.
- Initial fluid resuscitation should be done cautiously in a hyponatremic patient.
- In a patient with concurrent hypovolemia and hypo-osmolality, correction of volume deficit should take precedence over correction of osmolality.

Step 2: Take History and Perform Physical and Volume Status Examination

- This should be done to assess the severity of hyponatremia and the need for urgency of correction.
- Pay immediate attention to neurological symptoms such as headache, lethargy, obtundation, disorientation, drowsiness, impaired consciousness, or seizures irrespective of the duration of hyponatremia.
- Remember symptoms of hyponatremia depict neurological dysfunction induced by cerebral edema. Cerebral edema occurs due to a decrease in serum osmolality, which causes water movement into cells.
- Give attention to other symptoms of hyponatremia like anorexia, nausea, dizziness, and lack of balance.
- Examine previous records of serum sodium to assess chronicity.
- Chronic hyponatremia patients may appear to be asymptomatic despite a serum sodium concentration that is persistently below 120 mEq/L.
- Neurological symptoms are much less severe in chronic hyponatremia due to cerebral adaptation. They may present with nausea, fatigue, lethargy, dizziness, gait disturbances, forgetfulness, confusion, and muscle cramps.
- Seizures and coma are rarely seen in chronic hyponatremia and often reflect an acute deterioration of the hyponatremia.
- Ask for a history of electrolyte-rich fluid loss (vomiting, diarrhea, or diuretic therapy) that may point to hypovolemia.
- Ask for a history of excessive water intake.
- Elicit a history of low protein intake and/or high fluid intake.
- Look for a history of use of medications that cause hyponatremia, such as thiazide and thiazide-type diuretics, mannitol, desmopressin (dDAVP), intravenous immunoglobulin, and medications acting on the central nervous system, including some antidepressants, antiepileptics, and antipsychotics.
- Inquire and look for any symptoms and signs of adrenal deficiency or hypothyroidism.
- Ask for a history of hyponatremia.

- Look for a history consistent with malignancy, HIV, hepatic failure, or plasma cell dyscrasia or renal failure.
- Assess volume status. Look for signs of extracellular volume depletion, such as decreased skin turgor, a low jugular venous pressure, or orthostatic/persistent hypotension, which may be due to hypovolemia.
- Look for features of fluid overload such as pedal edema, ascites, and pleural effusion, which can be due to heart failure, cirrhosis, or renal failure.
- Determine the severity of symptoms, moderate or severe.
- Determine the need for hospitalization—a patient who develops acute symptoms with severe hyponatremia requires admission to the hospital.

Step 3: Assess the Severity of Hyponatremia

- Mild hyponatremia—130–134 mmol/L
- Moderate hyponatremia—120–129 mmol/L
- Severe hyponatremia—less than 120 mmol/L

Step 4: Approach to Hyponatremia and Finding Etiology (Fig. 1.1)

- Assess volume status, measure serum and urine osmolality, and measure spot urine sodium.
- Whenever hyperglycemia is present, correct the serum sodium concentration for the effect of glucose to identify the correct sodium level and exclude hypertonic hyponatremia. Correct Na using the formula: [Na + 2.4 (Glucose/100–1)].
- Plasma osmolality is normally around (280–295) mOsm/kg. It should always be measured for right interpretation, but can be calculated as follows:

$$\left[2\mathrm{Na} + \mathrm{Glucose}\left(\mathrm{in\,mg/dL}\right)/18 + \mathrm{BUN}\left(\mathrm{in\,mg/dL}\right)/2.8\right]$$

- Serum tonicity (effective serum osmolality) is the parameter sensed by osmoreceptors; serum tonicity controls the transcellular distribution of water. Water can freely cross almost all cell membranes and move from a lower tonicity area (higher water content) to an area of higher tonicity (lower water content).
- The main difference between tonicity and osmolality is that tonicity depicts the concentration of solutes that do not easily cross cell membranes (mostly sodium salts with a small contribution from glucose) and therefore controls the movement of water between cells and the extracellular fluid.
- On the other hand, osmolality also includes the osmotic contributions of urea and (if present) ethanol or other alcohols or glycols, which are considered

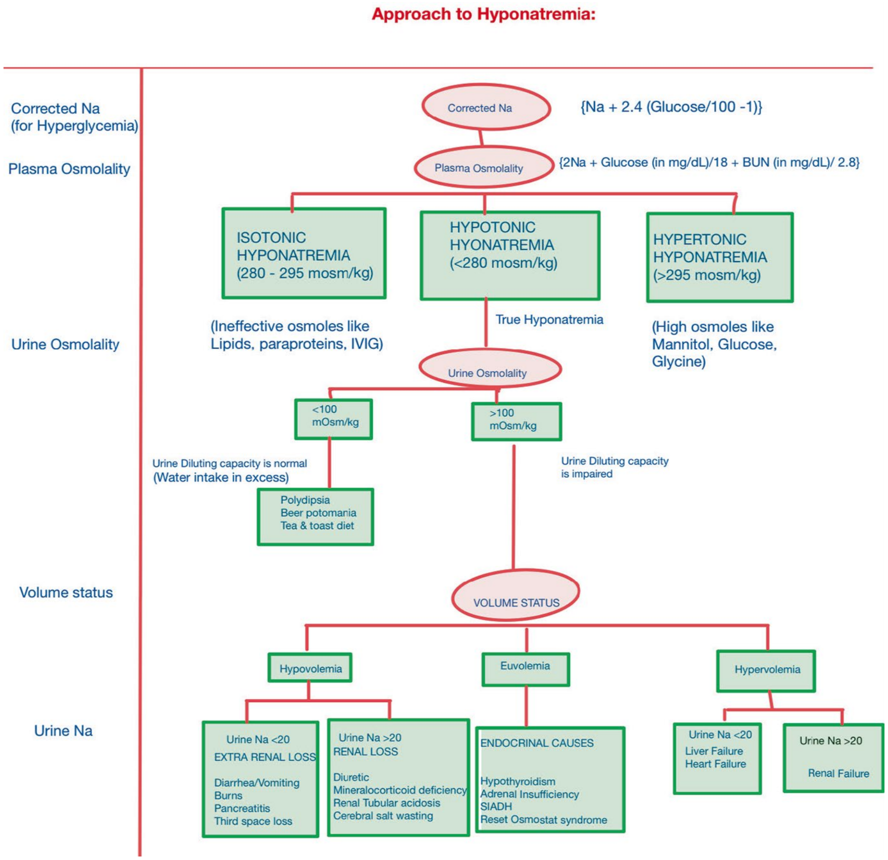
Approach to Hyponatremia:
Corrected Na (for Hyperglycemia)
Plasma Osmolality
Urine Osmolality
Volume status
Urine Na
Corrected Na
{Na + 2.4 (Glucose/100 -1)}
Plasma Osmolality
{2Na + Glucose (in mg/dL)/18 + BUN (in mg/dL)/ 2.8}
ISOTONIC HYPONATREMIA (280 - 295 mosm/kg)
HYPOTONIC HYONATREMIA (<280 mosm/kg)
HYPERTONIC HYPONATREMIA (>295 mosm/kg)
(Ineffective osmoles like Lipids, paraproteins, IVIG)
True Hyponatremia
(High osmoles like Mannitol, Glucose, Glycine)
Urine Osmolality
<100 mOsm/kg
>100 mOsm/kg
Urine Diluting capacity is normal (Water intake in excess)
Urine Diluting capacity is impaired
Polydipsia
Beer potomania
Tea & toast diet
VOLUME STATUS
Hypovolemia
Euvolemia
Hypervolemia
Urine Na <20
EXTRA RENAL LOSS
Diarrhea/Vomiting
Burns
Pancreatitis
Third space loss
Urine Na >20
RENAL LOSS
Diuretic
Mineralocorticoid deficiency
Renal Tubular acidosis
Cerebral salt wasting
ENDOCRINAL CAUSES
Hypothyroidism
Adrenal Insufficiency
SIADH
Reset Osmostat syndrome
Urine Na <20
Liver Failure
Heart Failure
Urine Na >20
Renal Failure

Fig. 1.1 An approach to hyponatremia

"ineffective" osmoles since they can pass freely and equilibrate across the cell membrane and therefore have little effect on water movement.

$$\text{Tonicity} = \text{measured serum osmolality} - \left(\text{BUN} / 2.8\right)$$

- All patients with true hyponatremia will have low serum osmolality.
- Isotonic hyponatremia (pseudohyponatremia) is where plasma osmolality is (280–295) mOsm/kg commonly due to ineffective osmoles like hyperlipidemia and paraproteinemia,
- Hypertonic hyponatremia is where plasma osmolality is more than 295 mOsm/kg. It results from the presence in extracellular fluid (ECF) of highly effective

osmoles other than sodium like mannitol, glucose, and glycerol. The osmotic pressure exerted by the non-sodium solute causes redistribution of water into ECF, leading to cellular dehydration and hyponatremia.

- Hypotonic hyponatremia (true hyponatremia) is where plasma osmolality is less than 280 mOsm/kg. This needs to be evaluated further with urine osmolality.
- Urine osmolality less than 100 mOsm/kg implicates normal diluting capacity of the renal system, so hyponatremia in such a situation is found in patients with polydipsia, Poor protein intake like malnutrition, beer potomania, tea, and toast diet.
- Urine osmolality of more than 100 mOsm/kg implicates impaired urine diluting capacity and is to be evaluated further with ECF volume status. Urine osmolality may be calculated using the last two digits of urine specific gravity × 30.
- Patients with lipemic serum, severe obstructive jaundice, or a known plasma cell dyscrasia may have pseudohyponatremia. This **laboratory artifact** occurs when sodium is measured with flame photometry.
- Look if the patient had recent surgery utilizing large volumes of electrolyte-poor irrigation fluid (e.g., prostate or intrauterine procedures) or treatment with mannitol, glycerol, or intravenous immunoglobulin, which causes iso-osmolar or hyperosmolar hyponatremia.
- Estimate serum creatinine concentration for glomerular filtration rate (GFR). Both severely reduced GFR and thiazide (or thiazide-type) diuretics are important causes of hypotonic hyponatremia.
- The volume status of the patient can guide us to further evaluate other causes.
  - **Hypervolemic hyponatremia** may present with edema, usually seen in patients with heart/liver/renal failure. Nonedematous patients with hypotonic hyponatremia are either euvolemic/hypovolemic.
  - **Euvolemic hyponatremia** is seen mostly with endocrinal disturbances like hypothyroidism, adrenocortical insufficiency, and drug-induced hyponatremia.
  - **Hypovolemic hyponatremia** can be associated with renal or extrarenal causes. This can be differentiated by taking urine Na levels. Most patients with hypovolemic hyponatremia exhibit clear signs of volume depletion; however, some hypovolemic patients may display more subtle signs, leading to a mistaken diagnosis of euvolemia.
  - Urine Na is found to be higher in renal causes like diuretics, and road traffic accident (RTA) (high in cerebral salt wasting as well). On the other hand, it has lower values in extrarenal causes like diarrhea, vomiting, burns, pancreatitis, and third space losses. These parameters are not applicable in patients receiving diuretics or having intrinsic renal disease.
- Initially investigations (serum and urine Na) (plasma and urine osmolality) can be sent for initial approach and aid in further assessment.

Step 5: Send Further Investigations

In addition to serum osmolality, urine osmolality, and urinary sodium, send further investigations to ascertain the cause and severity of hyponatremia.

- Serum K, Cl, bicarbonate
- Serum glucose, urea, creatinine, uric acid, total proteins, triglycerides
- Arterial blood gases
- Serum TSH, serum cortisol level
- Urine—creatinine, uric acid
- Fractionated excretion of sodium (FE Na) = (Urinary Na × Plasma Cr)/(Plasma Na × Urinary Cr) × 100

Step 6: Manage Hyponatremia (Fig. 1.2)

- **Correct serum sodium**
  - Hypertonic hyponatremia can be treated by removing the offending hyperosmolar agent like mannitol or glycine.
    - Isotonic hyponatremia is not clinically significant as it is an effect of ineffective osmoles and less likely to result in fluid shifts and cerebral edema.
    - Hypotonic hyponatremia, also called true hyponatremia, is what truly needs to be treated based on the duration/severity of symptoms.
  - Any patient with acute presentation (<48 h) or neurological symptoms needs to be actively treated.
- The treatment of hyponatremia in hospitalized patients has four objectives.
  - To prevent further decrease in the serum sodium concentration
  - To decrease intracranial pressure in patients at risk for developing brain herniation
  - To alleviate symptoms of hyponatremia
  - To avoid excessive correction of hyponatremia
- Treatment of hyponatremia depends on
  - Severity
  - Duration
  - Symptoms
  - Presence of pre-existing intracranial pathology
- The risk of cerebral edema is greater in acute hyponatremia and thus needs aggressive therapy.
- Chronic hyponatremia with lower serum sodium concentration has a greater risk of complications from overaggressive therapy and needs close monitoring to avoid overcorrection.

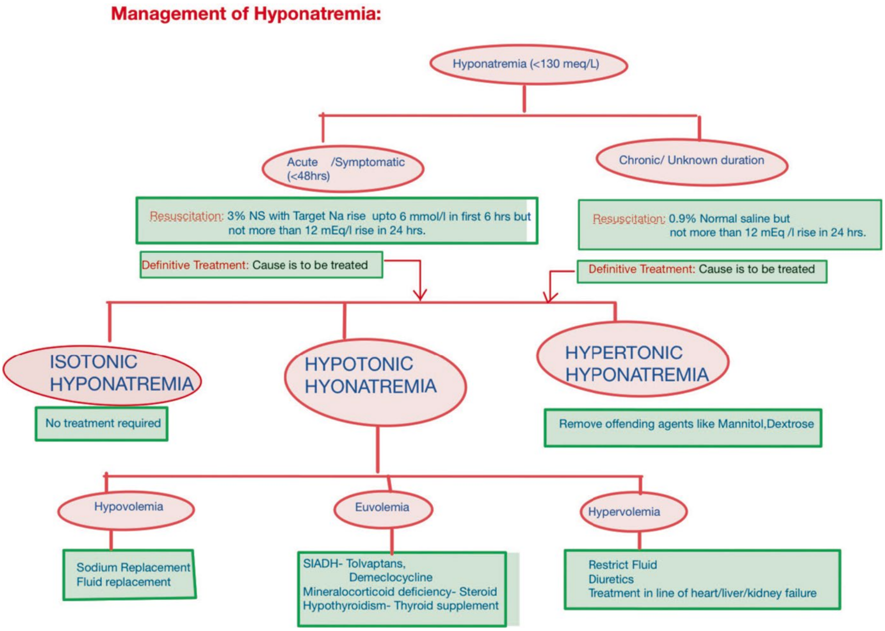
Management of Hyponatremia:
Hyponatremia (<130 meq/L)
Acute /Symptomatic (<48hrs)
Chronic/ Unknown duration
Resuscitation: 3% NS with Target Na rise upto 6 mmol/l in first 6 hrs but not more than 12 mEq/l rise in 24 hrs.
Resuscitation: 0.9% Normal saline but not more than 12 mEq /l rise in 24 hrs.
Definitive Treatment: Cause is to be treated
Definitive Treatment: Cause is to be treated
ISOTONIC HYPONATREMIA
No treatment required
HYPOTONIC HYONATREMIA
HYPERTONIC HYPONATREMIA
Remove offending agents like Mannitol,Dextrose
Hypovolemia
Sodium Replacement
Fluid replacement
Euvolemia
SIADH- Tolvaptans, Demeclocycline
Mineralocorticoid deficiency- Steroid
Hypothyroidism- Thyroid supplement
Hypervolemia
Restrict Fluid
Diuretics
Treatment in line of heart/liver/kidney failure

Fig. 1.2 Management of hyponatremia

Table 1.1 Risk factors of neurological complications in hyponatremia

Acute cerebral edema	Osmotic demyelination syndrome
Postoperative patients and young females	Too rapid correction of sodium Serum sodium less than 105 mEq/L Concurrent hypokalemia
Children	Malnourished patients
Psychiatric polydipsic patients	Alcoholics
	Burn patients
	Elderly women taking thiazides

- Patients with acute severe (i.e., serum sodium less than 120 mEq/L) symptomatic hyponatremia should be treated in hospital.
- Risks of treatment (osmotic demyelination) should be balanced against benefits (see Table 1.1). Too rapid correction of sodium is the most important risk factor for the development of osmotic demyelination syndrome.

Step 7: Choice of Fluid

- Patients with severe symptomatic hyponatremia should be treated with 3% hypertonic saline regardless of cause until resolution of symptoms.

- Plasma Na can be raised up to 4–6 mEq/L in the first 6 h or less in severely symptomatic patients. The same goal can be achieved over 24 h in less symptomatic patients. After the initial 3–4 h of rapid correction, the rate of correction should be slowed down. In patients with chronic severe hyponatremia, the maximum rate of correction should be 8 mEq/L in any 24 h.
- Asymptomatic patients can be treated with 0.9% normal saline with a target rise in plasma Na at the rate of 0.5 mEq/L/h but less than 10–12 mEq/L in 24 h as a more rapid elevation could lead to central pontine myelinosis.
- It is the daily change rather than the hourly rise of serum sodium that increases the risk of developing osmotic demyelination syndrome (ODS).

Step 8: Rate of Correction for Hyponatremia

- The quantity of sodium required to achieve the desired elevation in plasma Na,
- Sodium Deficit = Total Body Water (TBW) × (desired change in S.Na) where TBW = body weight (kg) × Y (Table 1.2).
  - For a 70-kg symptomatic man with plasma Na 105 mEq/L, the amount of sodium needed to raise plasma Na by 6 mEq/L in the first 6 h is
  - Sodium required = 0.6 × 70 × 6 = 252 mEq/L
- That is, approximately 500 mL 3%NS needed.
- Since 1000 mL of 3% NS has around 500 meq Na, so
  - 500 mL of 3% saline solution would be needed in the first 6 h, that is, 83 mL/h.
- A simpler approach is to calculate the amount of 3% hypertonic saline needed to raise serum sodium by 1 mEq/L, which is approximately 1 mL/kg of 3% hypertonic saline.
  - The rise in sodium should always be verified by repeated frequent serial measurements (4–6) hourly. These formulas are just an approximation that do not take into account the translocation of water, correction of the underlying cause, or ongoing water loss.

- **The current recommendations for correcting hyponatremia are as follows:**
  - Treat asymptomatic patients with a 50 mL bolus of 3% saline over 30 mins to prevent it from falling further. Avoid hypertonic saline if sodium is already autocorrecting.
  - Patients with features of increased intracranial pressure are given 100 mL of 3% saline followed by additional two boluses (300 mL total) if symptoms persist over 30 mins.

Table 1.2 Total body water in different population

	Children	Adult men	Adult women	Elderly men	Elderly women
Y =	0.6	0.6	0.5	0.5	0.45

- In chronic hyponatremia with mild-to-moderate symptoms but serum sodium <120 mEq/L, initiate 3% saline at a rate of 0.25 mL/kg/h, and in patients who are at a high risk of developing osmotic demyelination syndrome, simultaneously start desmopressin to prevent overly rapid correction.
- In chronic hyponatremia with mild-to-moderate symptoms and serum sodium >120 mEq/L water restriction less than the urine output volume and treat the underlying cause.

Step 9: Euvolemic, Hypo-Osmolar, Hyponatremia

Consider SIADH

- Clinical euvolemia.
- SIADH is the most common cause of hyponatremia in euvolemic patients with high urine osmolality (more than 300 mOsm/kg H_2O) and low serum osmolality less than 275 mOsm/kg H_2O.
- It is diagnosed after other etiologies are excluded.
- Urinary sodium concentration more than 40 mmol/L.
- Hypouricemia (less than 4 mg/dL L) due to increased urinary uric acid excretion and low blood urea nitrogen due to increased urea clearance.
- Normal renal, hepatic, adrenal, and thyroid function.
- **In severely symptomatic patients:**
  - Give 3% hypertonic saline to raise serum sodium by up to 6 mEq/L in the first 6 h.
  - The serum sodium should be measured frequently at 2–3 h, and the subsequent infusion rate should be adjusted to achieve a rate of correction of no more than 10- mEq/L in 24 h.
- **In asymptomatic and mildly symptomatic patients:**
  - Fluid restriction with the suggested intake of less than 800 mL/day is the mainstay of treatment in most patients with SIADH; do not restrict fluid in subarachnoid hemorrhage as it may induce cerebral vasospasm in such cases.
  - Fluid restriction is defined as the intake of fluid less than urinary output.
  - Oral salt tablets (1 gmNaCl =17 meq) can be administered.
  - Use intravenous saline like hypertonic saline, the electrolyte concentration of which must be greater than the electrolyte concentration of the urine.
  - Isotonic saline is infrequently effective and often leads to further lowering of the serum sodium.
  - Potassium is as osmotically active as sodium. So, giving potassium (usually for concurrent hypokalemia) can raise the serum sodium concentration and osmolality in hyponatremic patients. Intracellular sodium moves into the extracellular fluid in exchange for potassium and also extracellular chloride moves into the cells with potassium, so the increase in cell osmolality promotes free water entry into the cells and raises sodium.

- Loop diuretics may be added if urine output is very low and urine osmolality is more than twice the plasma osmolality (typically more than 550). Loop diuretics like furosemide inhibit sodium chloride reabsorption in the thick ascending limb of the loop of Henle interfere with the countercurrent mechanism and induce a state of antidiuretic hormone (ADH) resistance, resulting in the excretion of a less-concentrated urine and increased water loss.
- Consider vasopressin antagonist (vaptans) if no contraindications.
  - There are multiple receptors for the ADH vasopressin: the V1a, V1b, and V2 receptors.
  - The V2 receptors primarily mediate the antidiuretic response, while V1a and V1b receptors principally cause vasoconstriction and mediate adrenocorticotropic hormone (ACTH) release, respectively.
  - Some oral formulations, such as tolvaptan, mozavaptan, satavaptan, and lixivaptan, are selective for the V2 receptor.
  - Conivaptan blocks both the V2 and V1a receptors.
  - The vasopressin receptor antagonists produce a selective water diuresis (also called aquaresis) without affecting sodium and potassium excretion.
  - The free water loss will tend to correct the hyponatremia.
  - Thirst increases significantly with these agents, which may limit the rise in serum sodium.
  - Oral tolvaptan is available and recommended for use in these patients with hyponatremia due to SIADH. Dose 15 mg once daily to a maximum of 60 m daily.
  - These should be avoided in acute SIADH.
  - Tolvaptan should not be used for longer than 1 month and should not be given to patients with liver disease (including cirrhosis**).**
  - Conivaptan, V1a receptor blockade might worsen renal function in patients with cirrhosis since terlipressin, a V1a receptor agonist, has been used to treat hepatorenal syndrome.
- Demeclocycline can also be given in SIADH 600–1200 mg/day.
- In all cases of SIADH, correct the underlying cause and withdraw any offending drug.
- Other causes of euvolemic, hypo-osmolar hyponatremia such as hypothyroid, adrenal insufficiency, renal disease, and psychogenic polydipsia should be managed by water restriction, hormone replacement, and treatment of the underlying disease
- Hyponatremia with a reset osmostat pattern is a variant of the SIADH and should be suspected in any patient with mild-to-moderate hyponatremia (usually between 125 and 135 mEq/L) that is stable over time despite variations in sodium and water intake. The recommendations for SIADH do not apply to patients with reset osmostats. Treatment should be primarily directed at the underlying disease.

Step 10: Hypervolemic, Hypo-Osmolar, Hyponatremia

- It should be considered in edematous states such as cirrhosis, nephrotic syndrome, cardiac failure, and renal failure.
- Hyponatremic patients with heart failure or cirrhosis usually are in an advanced stage of the disease and present with clinically apparent peripheral edema and/or ascites.
- There is no evidence that correction of hyponatremia leads to improvement of hemodynamic disturbances or clinical outcomes associated with the underlying severe chronic heart failure.
- The main indications for specific therapy to correct hyponatremia are a serum sodium concentration below 120 mEq/L (severe hyponatremia) and/or the presence of symptoms that might be due to hyponatremia.
- **Cardiac failure with hyponatremia**
  - Restrict fluids
  - Give loop diuretics
  - Angiotensin inhibition with an angiotensin-converting enzyme (ACE) inhibitor or an angiotensin II receptor blocker (ARB) and a loop diuretic may be added to raise the serum sodium concentration.
  - Tolvaptan may have a role in the management of hyponatremia in patients with chronic heart failure when other management options have failed to increase the serum sodium above 120 mEq/L and/or ameliorate symptoms of hyponatremia.
  - Treat the underlying disease.
  - Avoid extra sodium.
- **Cirrhosis with hyponatremia**
  - Withdraw beta-blockers, alpha-blockers, diuretics (particularly thiazide diuretics).
  - Correct hypokalemia.
  - Treat patients who have persistent hypotension.
  - Midodrine is the agent typically used to increase blood pressure in cirrhotic patients.
  - In a severe symptomatic, attempt to raise the serum sodium with an infusion of albumin or hypertonic saline.
  - Hemodialysis can be done in advanced renal dysfunctions.

Step 11: Hypovolemic, Hypo-Osmolar, Hyponatremia

- Consider the volume-depleted state (renal or extrarenal).
- These should be managed by the following:
  - Volume replacement.
  - Treat the underlying disease.

  - Low urine sodium (<20 mEq/L)—the urine sodium is less than 20 mEq/L in patients with hypovolemia caused by gastrointestinal fluid losses (e.g., diarrhea), by the movement of fluid into the "third space" (e.g., pancreatitis).
  - High urine sodium (>40 mEq/L) with low urine chloride (<20 mEq/L) in hypovolemic hyponatremia patients can be present, who have metabolic alkalosis. This is caused by vomiting. There is a loss of bicarbonate in urine that negates the use of urine sodium as a marker of hypovolemia.
  - High urine sodium and chloride (>40 mEq/L)—the sodium and chloride concentrations are usually above 40 mEq/L in hypovolemic hyponatremic patients with renal salt losses.

Diuretic-Induced Hyponatremia

- This may mimic SIADH as it may be clinically euvolemic.
- Occurs predominantly with thiazide diuretics.
- May occur within a few days of starting diuretics.
- Elderly patients with a low body mass are more vulnerable.
- May be associated with increased water intake.
- Managed by stopping diuretics, isotonic or hypertonic saline, in symptomatic patients.
- At a high risk of rapid correction after stopping diuretics.
- Careful monitoring is required to avoid osmotic demyelination in these patients.
- Hyponatremic patients who present with clinical symptoms and signs of hypovolemia may have extrarenal fluid losses or renal fluid losses.
- Measurement of the urine sodium and chloride concentrations can often distinguish between these.
- Nonedematous patients with hypotonic hyponatremia are either euvolemic or hypovolemic.
- Sometimes both SIADH and thiazide-induced hyponatremia may be present due to the underlying disease and diuretic used, respectively.

Cerebral Salt Wasting (CSW)

- This may mimic SIADH as laboratory findings are similar but the management is very different. There is a need for fluid restriction in SIADH in contrast to the need for fluid replenishment in CSW.
- Hyponatremia with a low plasma osmolality.
- An inappropriately elevated urine osmolality (>100 mOsm/kg and usually >300 mOsm/kg).
- A urine sodium concentration above 40 mEq/L.
- Much less common than SIADH.
- Occurs with acute CNS disease, mainly subarachnoid hemorrhage.
- Clinically hypovolemic.
- Normal serum uric acid.
- Increased fractional excretion of urate.

Table 1.3 Differentiating SIADH from CSW

	CSW	SIADH
Plasma volume	Decreased	Normal or increased
Salt balance	Negative	Normal
H_2O balance	Negative	Increased or no change
Signs of dehydration	Present	Absent
Weight	Decreased	Increased or no change
PCWP and CVP	Decreased	Increased or normal
Hematocrit	Increased	Increased or normal
BUN/creatinine ratio	Increased	Normal
Serum protein concentration	Increased	Normal
Serum K concentration	Increased or no change	Decreased or no change
Serum uric acid concentration	Normal	Decreased

PCWP pulmonary capillary wedge pressure, *CVP* central venous pressure, *BUN* blood urea nitrogen

- This can be differentiated from SIADH as mentioned in Table 1.3.
- Management
  - Treat the underlying causes of CSW like subarachnoid hemorrhage.
  - Put the central line.
  - Volume replacement—match urine loss.
  - Amount of sodium required = sodium deficit × total body water.
  - Blood product if anemia is present.

Step 12: Hyperosmolar Hyponatremia

- Consider hypertonic mannitol, glycine, or other osmotic agents and hyperglycemia.
- Patients with recent prostate or uterine surgery. The absorption of nonconductive glycine, sorbitol, or mannitol irrigation solutions during TURP of the prostate or bladder or hysteroscopy or laparoscopic surgery can lower the serum sodium by escalating the extracellular fluid volume along with these sodium-free solutions.
- Treatment
  - Stop infusion.
  - Hyperglycemia—stop or decrease glucose administration.
  - Give insulin and fluids.
  - Target a drop in glucose concentration of 75–100 mg/dL/h.

Step 13: Iso-Osmolar Hyponatremia

- Consider pseudohyponatremia (drip arm sample, hyperlipidemia, paraproteinemia, plasma cell dyscrasia, and patients with obstructive jaundice.
- Usually, asymptomatic.
- No treatment is required.

Case Vignette for the Management of Hyponatremia (Tables 1.4, 1.5, 1.6, 1.7, 1.8, and 1.9)

Table 1.4 Case 1

1. A 70 kg diabetic man presents with polyuria, serum Na 130 mEq/L, BUN 18, and urine osmolality 220 mOsm/kg. His RBS was found to be 400 mg/dL.	
Glucose	400
Corrected Na	Na + 2.4 [(Glu/100)-1] 130 + 2.4[(400/100)-1] 137.2 Normonatremic

Table 1.5 Case 2

2. An 80 kg woman presents with nausea, loss of appetite, and weakness. She has no signs of dehydration as such. On evaluation, she has serum Na 130 mEq/L, RBS 120 mg/dL, BUN 10, urine osmolality 160 mOsm/kg, and urine Na 45. How do we approach this case?	
Glucose	120
Corrected Na	Na + 2.4 [(Glu/100)−1] 130 + 2.4[(120/100)−1] 130.48 Hyponatremic
Plasma osmolality	2Na + Glu/18 + BUN/2.14 [(2 × 130) + (120/18) + (10/2.14)] 270.7 Hypotonic hyponatremia
Urine osmolality	160 Impaired water excretion as Uosm>100
Volume status	Not suggestive of dehydration or fluid overload
Urine Na	45
Diagnosis	SIADH
Management	Fluid restriction Treat underlying cause Cautious use of tolvaptan

Table 1.6 Case 3

3. An 80 kg female case of road traffic accident with intracranial hemorrhage presents to ER with BP of 100/60 mmHg with high urine output. On evaluation, she has serum Na 130 mEq/L, RBS 135 mg/dL, BUN 10, urine osmolality 160 mOsm/kg, and urine Na 250. IVC diameter is < 2 cm with more than 50% collapsibility. What is your diagnosis?	
Glucose	135
Corrected Na	Na + 2.4 [(Glu/100)-1] 130 + 2.4[(135/100)-1] 130.84 Hyponatremic
Plasma osmolality	2Na + Glu/18 + BUN/2.14 [(2 × 130) + (135/18) + (10/2.14)] 272.17 Hypotonic hyponatremia
Urine osmolality	160 Impaired water excretion as Uosm>100
Volume status	Hypovolemic
Urine Na	250
Diagnosis	Cerebral wasting syndrome (CSW)
Management	Isotonic saline

Table 1.7 Case 4

4. A 55 kg man presents with fever, abdominal cramps, vomiting, loose motion, and decreased urine output for three days. He has sunken eyes, dry tongue, and poor skin turgor. On evaluation, he has S Na 128 mEq/L, RBS 120 mg/dL, BUN 10, urine osmolality 180 mOsm/kg, and urine Na 15. What is your diagnosis?	
Glucose	120
Corrected Na	Na + 2.4 [(Glu/100)-1] 128 + 2.4[(120/100)-1] 128.48 Hyponatremic
Plasma osmolality	2Na + Glu/18 + BUN/2.14 [(2 × 128) + (120/18) + (10/2.14)] 267.33 Hypotonic hyponatremia
Urine osmolality	180 Impaired water excretion as Uosm>100
Volume status	Dehydrated, hypovolemic
Urine Na	15
Diagnosis	GI cause, probably acute gastroenteritis
Management	Fluid and electrolyte resuscitation

Table 1.8 Case 5

5. A 70 kg man presented with headache, confusion, and nausea for the past 36 h. On evaluation, serum Na is 110 mEq/L and RBS 124 mg/dL.	
Symptoms?	Symptomatic
Choice of fluid	3% NS till resolution of symptoms
Rate of correction	Up to 6 mEq/L in first 6 h (but 8 meq/L in 24 h)
Sodium deficit	TBW × (target change in serum Na) (0.6 × 70) × 6) 250 mEq/L
3% NS	1000 mL of 3% NS contains about 500 mEq Na
	500 mL of 3%NS over 6 h 80 mL/h of 3%NS for 6 h

Table 1.9 Case 6

6. A 65 kg woman was referred from another hospital with a fall in serum Na to 110 mEq/L in 24 h, although with no symptoms. Her RBS was found to be 142 mg/dL.	
Symptoms?	Asymptomatic
Choice of fluid	3%NS (as acute severe hyponatremia)
Rate of correction	10 mEq/L over 24 h
Sodium deficit	TBW × (target change in serum Na) (0.6 × 70) × 10) 420 mEq/L
3% NS	1000 mL of 3% NS contains about 500 mEq Na, so 2 mL (double) of 3%NS will be required to replace 1 mEq Na
	840 mL over 24 h 35 mL/h for 24 h

Suggested Reading

Adrogue HJ, Madias NE. Hyponatremia. N Engl J Med. 2000;342:1581–9. *Pictorial description of extracellular fluid and intracellular fluid compartments under normal conditions and during states of hyponatremia*

Ferguson-Myrthil N. Novel agents for the treatment of hyponatremia: a review of conivaptan and tolvaptan cardiology in review. Cardiol Rev. 2010;18(6):313–21. *The article describes the role of conivaptan and tolvaptan in the treatment of hyponatremia*

Irwin RS, Rippe JM. Irwin and Rippe's intensive care medicine. 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2006. p. 898–912.

Spasovski G, Vanholder R, Allolio B, et al. Clinical practice guideline on diagnosis and treatment of hyponatraemia. Eur J Endocrinol. 2014;170:G1. *Guidelines for hyponatrmia*

Sterns RH. Treatment of severe hyponatremia. Clin J Am Soc Nephrol. 2018;13:641. *A review article*

Verbalis JG, Goldsmith SR, Greenberg A, Schrier RW, Sterns RH. Hyponatremia treatment guidelines 2007: expert panel recommendations. Am J Med. 2007;120(11A):S1–S21. *A comprehensive guideline-based approach for the management of hyponatremia*

Hypernatremia

2

Rajesh Chawla, Subhash Todi, Raju Shakya,
and Aakanksha Chawla

> A 75-year-old male patient, a case of chronic obstructive pulmonary disease (COPD), was transferred from another hospital with complaints of fever, increased breathlessness for 5 days, and altered sensorium for 1 day. He also had an episode of seizure 1 day. He was being managed as an acute exacerbation of COPD with cor pulmonale and pneumonia. He received antibiotics and diuretic therapy in the previous hospital. On evaluation, his laboratory values showed hemoglobin 13 g/dL, packed cell volume of 38.5%, serum sodium 160 mEq/L, serum potassium 3.0 mEq/L, serum urea 146 mg/dL, and serum creatinine of 1 mg/dL.

Hypernatremia is a common problem characterized by a rise in serum sodium above 145 mEq/lt. This condition is caused by a decrease in total body water relative to the sodium content. Normally it gets corrected due to thirst and increased water intake.

- It is important to understand the changes in extracellular fluid (ECF) and intracellular fluid (ICF) compartments during normal states and states of hypernatremia (Fig. 2.1).

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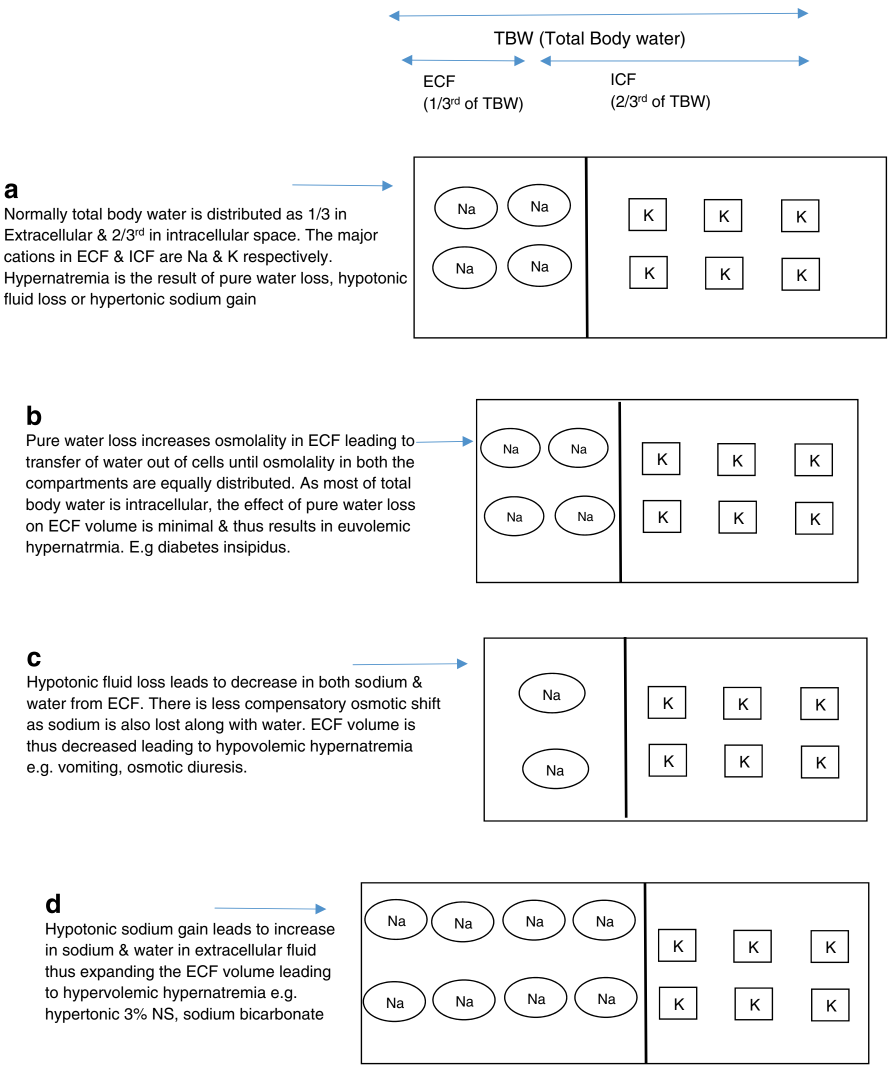

a
Normally total body water is distributed as 1/3 in Extracellular & 2/3rd in intracellular space. The major cations in ECF & ICF are Na & K respectively. Hypernatremia is the result of pure water loss, hypotonic fluid loss or hypertonic sodium gain

b
Pure water loss increases osmolality in ECF leading to transfer of water out of cells until osmolality in both the compartments are equally distributed. As most of total body water is intracellular, the effect of pure water loss on ECF volume is minimal & thus results in euvolemic hypernatrmia. E.g diabetes insipidus.

c
Hypotonic fluid loss leads to decrease in both sodium & water from ECF. There is less compensatory osmotic shift as sodium is also lost along with water. ECF volume is thus decreased leading to hypovolemic hypernatremia e.g. vomiting, osmotic diuresis.

d
Hypotonic sodium gain leads to increase in sodium & water in extracellular fluid thus expanding the ECF volume leading to hypervolemic hypernatremia e.g. hypertonic 3% NS, sodium bicarbonate

Fig. 2.1 Extracellular and intracellular fluid compartment during normal conditions and during hypernatremia

- As depicted in Fig. 2.1a, total body water is normally distributed as one-third in extracellular and two-thirds in intracellular space, where Na and K are the major cations in ECF and ICF, respectively. Hypernatremia can occur either due to pure water loss, hypotonic fluid loss, or hypertonic sodium gain.
- As in Fig. 2.1b, in conditions with pure water loss, there is an increase in extracellular fluid (ECF) osmolality, leading to the transfer of water out of cells until osmolality in both compartments is equally distributed. As most of the total body

water is intracellular, the effect of pure water loss on ECF volume is minimal and thus results in euvolemic hypernatremia, for example, diabetes insipidus.
- As in Fig. 2.1c, hypotonic fluid loss leads to a decrease in both sodium and water from ECF. There is less compensatory osmotic shift as sodium is also lost along with water. ECF volume is thus decreased leading to hypovolemic hypernatremia, for example, vomiting and osmotic diuresis.
- As seen in Fig. 2.1d, hypertonic sodium gain leads to an increase in sodium and water in extracellular fluid, thus expanding the ECF volume and leading to hypervolemic hypernatremia, for example, hypertonic 3% NS and sodium bicarbonate.

The goal of management involves identifying hypernatremia and correcting volume disturbances and hypertonicity.

Grades of hypernatremia:

Mild: (145–150) mEq/L
Moderate: (151–170) mEq/L
Severe: (>170) mEq/L

Step 1: Initiate Resuscitation (Refer Chap. 24)

- Assess and secure the airway and provide ventilatory support when required.
- Differentiate between hypovolemia, which is due to water and sodium loss, and dehydration, which is predominantly due to water loss
- Infuse isotonic sodium chloride in hypovolemic patients.

Step 2: Take History and Perform a Physical Examination

- This should be done to assess the etiology of hypernatremia and the severity of the problem.
- Look for symptoms suggestive of hypernatremia (Table 2.1). These are nonspecific and may even mimic the rapid fall of serum sodium.
- History should be taken focusing on the following problems:
  - Extrarenal fluid losses (e.g., burns, vomiting, diarrhea, fever, high minute ventilation in mechanically ventilated patients)

Table 2.1 Clinical features suggestive of hypernatremia

Central nervous system			
Anorexia	Restlessness	Confusion	Weakness
Lethargy	Seizure	Respiratory failure	Coma
Musculoskeletal symptoms			
Twitching	Hyperreflexia	Ataxia	Tremor

  - Decreased fluid intake
  - Polyuria (i.e., signs of diabetes insipidus [DI] or osmotic diuresis)
  - Review drug chart (drugs causing DI, osmotic diuretics, osmotic laxatives, glycosuria)
  - Review previous sodium levels to assess chronicity
  - Hypertonic solution infusion (sodium bicarbonate, hypertonic saline, total parenteral nutrition)
  - Hypertonic feed (high-protein formula, concentrated formula)

Step 3: Assess Volume Status

- This is important to understand the underlying pathophysiology of hypernatremia (Table 2.2) and plan the treatment strategy.
- Volume status can be assessed by clinical means, hemodynamic monitoring, and urine biochemistry (Table 2.3).

Table 2.2 Pathophysiology of hypernatremia

Hypovolemic (i.e., water deficit > sodium deficit)
Extrarenal losses—diarrhea, vomiting, fistulas, significant burns
Renal losses
Osmotic diuretics (glycosuria, urea diuresis due to catabolism, recovery from renal failure, mannitol)
Diuretics
Postobstructive diuresis
Intrinsic renal disease (renal tubular disease)
Adipsic hypernatremia is secondary to decreased thirst
Damaged hypothalamic thirst centers
Hypervolemic (i.e., sodium gain > water gain)
Hypertonic saline
Sodium bicarbonate administration
Accidental salt ingestion (e.g., error in preparation of infant formula)
Mineralocorticoid excess (Cushing's syndrome)
Net sodium gain treating hypotonic fluid loss mainly water loss by isotonic normal saline and subsequently giving loop diuretics for edema
Euvolemic
Extrarenal losses—increased insensible loss (e.g., hyperventilation)
Renal losses—Arginine arginine vasopressin deficiency or resistance (formerly called central DI, nephrogenic DI)
Mostly free water loss is from intracellular and interstitial spaces

Table 2.3 Assessment of low-volume status

A. *Clinical*
Increasing thirst
Dry tongue, sunken eyes, reduced skin turgor on the forehead and sternal skin
Orthostatic tachycardia (>20/min rise of pulse rate)
Orthostatic hypotension (>20 mmHg fall in systolic BP or >10 mmHg fall in diastolic BP)
Resting tachycardia and hypotension
Low urine output, concentrated urine (extrarenal loss)
B. *Hemodynamic*
Low central venous pressure
Arterial pressure variation (in ventilated patients)
Rising arterial pressure on passive leg raising (spontaneously breathing patients)
C. *Biochemistry*
Rising hematocrit
Rising albumin
Raised urea in proportion to serum creatinine
High serum uric acid
High urine osmolarity
Low urine sodium (extrarenal loss)
Low urine chloride (metabolic alkalosis)

Step 4: Send Investigations

- Arterial blood gases and serum electrolytes
  - Blood glucose, blood urea, serum creatinine, and uric acid
- Serum osmolality and urine osmolality
- Urinary sodium and chloride
- If indicated, do imaging studies: head CT scan or MRI

Step 5: Approach to Hypernatremia (Fig. 2.2)

- Serum osmolality is always increased in patients with hypernatremia.
- *The volume status* of patients is to be assessed.
  - *Hypovolemia* is seen in case of water loss from the gastrointestinal, renal tract or skin.
  - *Hypervolemia* is common in patients with hypertonic saline and sodium bicarbonate. It is also seen with hyperaldosteronism and Cushing's syndrome.
  - *Euvolemic* patients are to be further evaluated with urine osmolality.

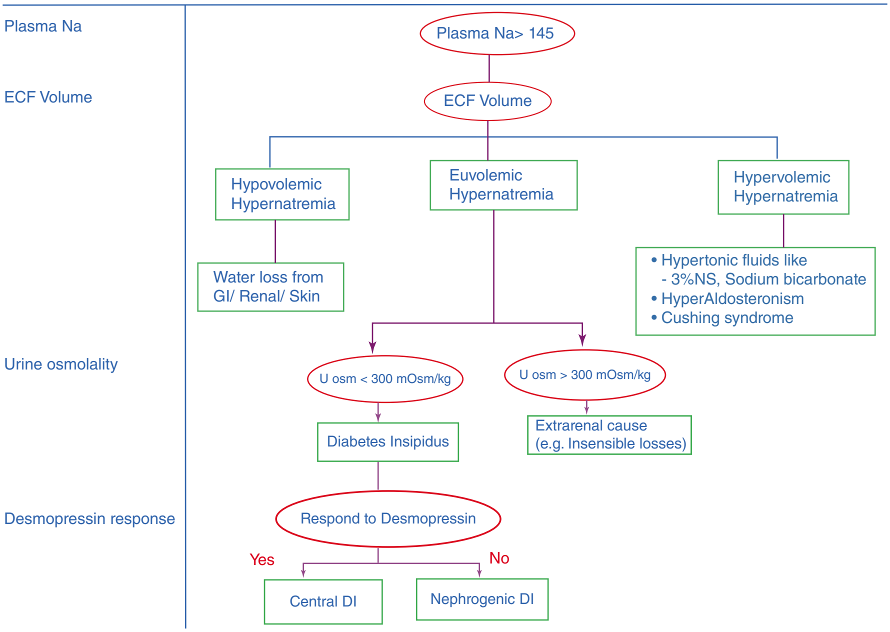
Plasma Na
ECF Volume
Urine osmolality
Desmopressin response
Plasma Na> 145
ECF Volume
Hypovolemic Hypernatremia
Euvolemic Hypernatremia
Hypervolemic Hypernatremia
Water loss from GI/ Renal/ Skin
• Hypertonic fluids like
- 3%NS, Sodium bicarbonate
• HyperAldosteronism
• Cushing syndrome
U osm < 300 mOsm/kg
U osm > 300 mOsm/kg
Diabetes Insipidus
Extrarenal cause (e.g. Insensible losses)
Respond to Desmopressin
Yes
No
Central DI
Nephrogenic DI

Fig. 2.2 Approach to hypernatremia

- *Urine osmolality* in euvolemic hypernatremic patients can aid in further diagnosis.
  - Urine osmolality of less than 300 mOsm/kg is seen in diabetes insipidus. Central DI responds to desmopressin while nephrogenic DI does not respond to this.
  - Urine osmolality of more than 300 mOsm/kg can be seen with extrarenal causes like insensible losses.
- Urine osmolality of 300–600 mOsmols/kg may be due to osmotic diuresis (check for glycosuria).
- Calculate total solute excretion (urine osmolality × urine volume); if more than 1000 models per day—osmotic diuresis.

Step 6: Treatment

- The therapeutic approach depends on the rapidity at which hypernatremia has developed, its symptoms, and whether or not it has occurred due to the correction of severe hyperglycemia.
- Aim for symptom resolution, 10–15% improvement in sodium levels in the first 24 h.

- Correction in chronic hypernatremia (present for more than 48 h) settings:
  - Total sodium correction should be less than (10) mEq/24 h
- Rapid correction will cause a rapid shift of water inside the brain, causing cerebral edema and seizures.

Step 7: Calculate Water Deficit (Table 2.4)

$$\text{Water deficit}\left(\text{L}\right) = \text{total body water}\left(\text{TBW}\right)\times\left[\left(\text{measured Na}/140\right)-1\right]$$

$$\text{TBW} = \text{body weight}\left(\text{Kg}\right)\times{}^{''}\ \text{Y}''$$

For example:

- 60 kg adult woman with serum sodium of 160 mEq/L. Desired sodium is 140 mEq/L.
- Free water deficit = [(0.5 × 60)] × [(160/140) − 1] = 4.2 L.
- This can be given as 5% dextrose or free water through the nasogastric tube or orally.
- Free water deficit = 4.2 L (see above).
- Thus, a 4.2-L positive water balance must be achieved to get serum sodium down from 160 to 140 mEq/L or by 20 mEq.
- Rate of correction = 0.5 mEq/h.
- 4.2 L of free water to be given over 40 h at a rate of approximately 100 mL/h.
- Insensible water loss (30 mL/h) should be added.
- Thus, 130 mL/h of free water needs to be replaced for 40 h.
- This can be done with IV 5% dextrose, 0.45% saline, or plain water by the tube or orally.
- A large volume of 5% dextrose will lead to hyperglycemia, and if needed, insulin should be given to prevent glycosuria, otherwise osmolar diuresis can worsen hypernatremia.
- Sodium and/or potassium can be added to the intravenous fluid as necessary to treat concurrent volume depletion and/or hypokalemia (e.g., due to diarrhea).
- The addition of solutes decreases the amount of free water that is being given.
- If potassium is also added, then even less free water is present and a further adjustment to the rate must be made.
- Repeat sodium level and entire calculation every 12 h and replan infusion rate. (This is because the urinary free water loss is not taken into account and it keeps on changing.)

Table 2.4 Percentage of body water in body weight

Y = children	Adult men	Adult women	Elderly men	Elderly women
0.6	0.6	0.5	0.5	0.45

This is the percentage of water in total body weight

- In general, a net positive balance of 3 mL of electrolyte-free water per kg body weight will decrease serum sodium by 1 mEq/L.
- Initially 5% dextrose at the rate of 3–5 mL/kg/h should be infused, which should be reduced to 1 mL/kg/h once serum sodium normalizes.
- The current recommendation is to give 5% dextrose in water intravenously at a rate of 1.35 mL/h/kg body weight up to a maximum of 150 mL/h or approximately 70 mL/h in a 50 kg patient and 100 mL/h in a 70 kg patient.
- Additional free water is needed for ongoing urinary or gastrointestinal loss and also obligatory losses from skin and stool.
- Due to the above reason, free water correction based solely upon calculated water deficit will produce rate of correction less than 10 mEq/L/day.
- These calculations are only approximations, and frequent sodium and glucose measurements every 4–6 h should be performed till serum sodium is 146 mEq/L.

Step 8: Manage Specific Hyponatremic States (Table 2.5)

The management of specific hyponatremic states according to volume status is described in Table 2.5.

Table 2.5 Management of hypernatremia and volume status (Fig. 2.3)

Hypovolemic hypernatremia	Volume deficit always takes precedence over correcting water deficit
	Correct volume deficit initially by isotonic saline until improvement of orthostasis, tachycardia, and urine output
	Calculate and correct water deficit
	Treat the etiology of volume loss
	After correction of volume deficit, administer 0.45% saline, 5% dextrose, or oral water, replacing deficit and ongoing losses
Euvolemic hypernatremia	Correct water deficit
	Administer 0.45% saline, 5% dextrose, or oral water, replacing deficit and ongoing losses
	Follow serum [Na] carefully to avoid water intoxication
	Central DI—treat the underlying disease, long-term nasal pitressin or desmopressin
	Nephrogenic DI—correct calcium, potassium; remove offending drugs; low-sodium diet
Hypervolemic hypernatremia	Remove the source of extra sodium
	Correct the cause
	Loop diuretics alone can worsen hypernatremia; thus, combining with metolazone or thiazide diuretics will be a better choice
	Hemodialysis may be performed in renal failure

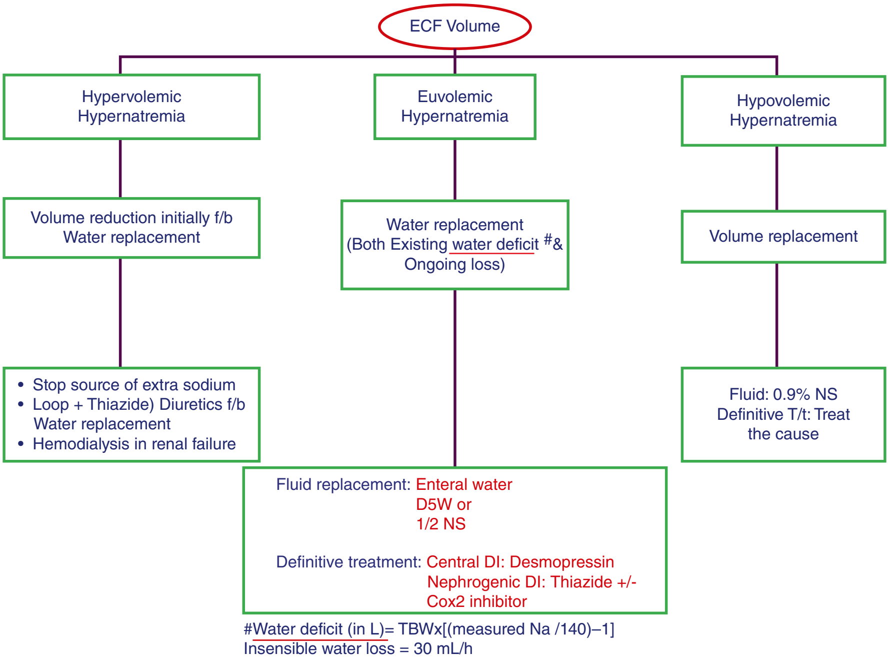
ECF Volume
Hypervolemic Hypernatremia
Euvolemic Hypernatremia
Hypovolemic Hypernatremia
Volume reduction initially f/b Water replacement
Water replacement (Both Existing water deficit #& Ongoing loss)
Volume replacement
• Stop source of extra sodium
• Loop + Thiazide) Diuretics f/b Water replacement
• Hemodialysis in renal failure
Fluid: 0.9% NS
Definitive T/t: Treat the cause
Fluid replacement: Enteral water
D5W or
1/2 NS
Definitive treatment: Central DI: Desmopressin
Nephrogenic DI: Thiazide +/- Cox2 inhibitor
#Water deficit (in L)= TBWx[(measured Na /140)–1]
Insensible water loss = 30 mL/h

Fig. 2.3 Management of hypernatremia

Suggested Reading

Adeleye O, Faulkner M, Adeola T, ShuTangyie G. Hypernatremia in elderly. J Natl Med Assoc. 2002;94:701–5. *It describes the risk factors, pathophysiology, causes, prevention, and management of hypernatremia in the elderly*

Adrogue HJ, Madias NE. Hyponatremia. N Engl J Med. 2000;342:1493–9. *It describes extracellular fluid and intracellular fluid compartments under normal conditions and during states of hypernatremia. It also elaborates the list of etiological factors*

Chauhan K, Pattharanitima P. Rate of correction of hypernatremia and health outcomes in critically ill patients. Clin J Am Soc Nephrol. 2019;14(5):660–3. *Treatment guidelines for correction of hypernatremia*

Lin M, Liu SJ, Lim IT. Disorders of water imbalance. Emerg Med Clin N Am. 2005;23:749–70. *Comprehensive review and pictorial description of management of sodium and water imbalance*

Lindner G, Funk GC. Hypernatremia in critically ill patients. J Crit Care. 2013;28(2):216.e11–20. *A review article on hypernatremia*

Nguyen MK. Quantitative approaches to the analysis and treatment of the dysnatremias. Semin Nephrol. 2009;29(3):216–26. *Formula-based approach for hypernatremia*

Sterns RH. Disorders of plasma sodium–causes, consequences, and correction. N Engl J Med. 2015;372(1):55–65. *Review article on sodium*

Hypokalemia and Hyperkalemia

3

Subhash Todi and Rajesh Chawla

Case Vignette

A 50-year-old male patient was admitted with generalized weakness and abdominal distension. On examination, he was found to be alert and hemodynamically stable. Neurological examination revealed quadriparesis. Abdominal examination revealed distension with sluggish bowel sounds. His serum potassium level was 2 mEq/L.

Disorder of potassium balance—both hypo- and hyperkalemia—is a common finding in the ICU. These abnormalities might be subtle, requiring minimal intervention, or life-threatening, requiring urgent measures. A methodological approach is warranted to manage this problem.

Step 1: Initial Resuscitation

- Patients should be resuscitated, as mentioned in Chap. 19, vol. 1.
- Patients with severe muscle weakness due to hypokalemia need to be assessed for airway protection and respiratory failure and if needed should be intubated and ventilated.
- Circulatory status needs to be maintained with intravenous fluids as hypokalemic patients are usually volume depleted.

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Step 2: Assess the Severity of Hypokalemia

- After initial resuscitation, the patient should be assessed for urgency of correction of hypokalemia.
- Urgent intravenous correction is needed in the following conditions:
  - ECG changes in hypokalemia (see Table 3.1 and Fig. 3.1).
- Cardiac arrhythmia.
- Previous long QT interval.
- Severely impaired neuromuscular function.
- Diaphragmatic weakness and respiratory failure.
- Patients on digoxin or antiarrhythmic therapy.
- Old age.
- Organic heart disease.
- Serum potassium of less than 3.0 mEq/L.
- Diabetic ketoacidosis.
- Hyperosmolar nonketotic diabetes.

Table 3.1 ECG changes in hypokalemia

ST segment depression
Decrease in amplitude of T waves
Increase in amplitude of U wave (occurring at the end of T)
Premature atrial or ventricular ectopics
Sinus bradycardia
Paroxysmal atrial or junctional tachycardia
Atrioventricular block
Ventricular tachycardia (torsade de pointes)
Ventricular fibrillation

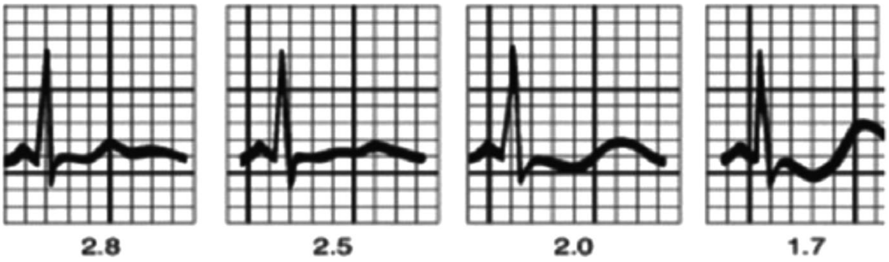

Fig. 3.1 Hypokalemia

Step 3: Estimate Potassium Deficit

- Approximately 200 mEq potassium deficit is required to decrease serum potassium by 1 mEq/L in the chronic hypokalemic state.
- In acute situations, the serum potassium concentration falls by approximately 0.27 mEq/L for every 100 mEq reduction in total body potassium stores.
- This is only an approximation, and careful monitoring of serum potassium is required.
- This approximation only takes into consideration potassium deficit but does not account for ongoing losses or intracellular shifts and daily maintenance requirement of potassium.
- Daily requirement of potassium is 40–120 meq/day.

Step 4: Replace Intravenous Potassium Chloride (Table 3.2)

Table 3.2 Replacement of potassium chloride by intravenous route (Table 3.2)

Peripheral route
It is safe One vial (10 mL) of potassium chloride contains 20 mEq of potassium.
It is used in mild-to-moderate hypokalemia (3–3.5 mEq/L).
20–40 mEq/L of KCl is added to each liter of fluid given over 4–6 h.
A saline rather than dextrose solution should be used. Half-strength saline with 20 mEq of KCl makes the solution isotonic and suitable for peripheral use.
Do not use high concentrations over 60 mEq/L; it can lead to pain and sclerosis of the peripheral vein. For small volume infusion of 100–200 mL, 10 mEq of potassium may be added.
Volume overload is a potential risk in susceptible subjects. Beware of rebound hyperkalemia after potassium replacement in patients with redistribution hypokalemia. In patients with redistributive hypokalemia due to increased sympathetic tone (e.g., redistr in thyrotoxic periodic paralysis, addition of nonselective beta-blockers like propranolol can rapidly reverse hypokalemia and associated symptoms).
Central route (it is used in severe hypokalemia 2.5–3 mEq/L)
Prepare 20 mEq KCl in 50 to 100 mL normal or half-strength saline.
5–20 mEq/h (through syringe pump) can be safely given by central route (preferably femoral vein). Repeat every 4 h depending on the serum potassium level. Potassium phosphate should be considered as a replacement in patients with concomitant hypophosphatemia due to refeeding syndrome.
Life-threatening arrhythmias
Up to 40 mEq/h of KCl can be given for a few hours.
No other infusion should be going through the same catheter.
Avoid blood sampling and flushing the catheter.
Frequently monitor potassium till 3–3.5 mEq/L.
Continuous ECG monitoring is required.

Step 5: Replace Intravenous Magnesium

- Hypomagnesemia is usually concurrently present with hypokalemia and needs to be corrected.
- Patients with hypomagnesemia may be refractory to potassium replacement alone.

Step 6: Ascertain the Cause of Hypokalemia and Manage it Specifically (Table 3.3)

- Detailed history and physical examination should be performed to look for systemic causes of hypokalemia.
- History of increased urinary or gastrointestinal loss of fluid (vomiting, diarrhea, polyuria) should be taken.
- Detailed drug history to rule out drug-induced hypokalemia should also be taken.
- Urinary potassium level of more than 30 mEq/day is a feature of loss of potassium in the urine.
- This can be calculated by the following:
  - 24 h urine collection and measuring potassium concentration.

Table 3.3 Causes of hypokalemia

Increased entry into cells (redistributive hypokalemia)
Metabolic alkalosis
DKA or HONK after insulin replacement
Elevated β-adrenergic activity—Stress or administration of β-agonists
Hypokalemic periodic paralysis
Refeeding syndrome
Hypothermia
Chloroquine intoxication
(Increase loss: Gastrointestinal)
Vomiting
Diarrhea
Nasogastric tube drainage
Laxative abuse
Increased urinary losses
Diuretics
Primary mineralocorticoid excess
Hypomagnesemia
Amphotericin B
Salt-wasting nephropathies—Including Bartter's or Gitelman's syndrome
Renal tubular acidosis, polyuria
Other
Dialysis
Plasmapheresis
Increased sweating
Decreased potassium intake (rare)

  - Spot urinary potassium: less than 15 mEq/L suggest nonurinary cause of hypokalemia.
  - Sending a spot sample of potassium in urine and multiplying it by 24 h urine output (e.g. if spot sample is 10 mEq/L and 24 h urine is 1 L, then 24 h urinary potassium loss is 10 mEq and denotes that hypokalemia is not due to urinary loss but due to an intracellular shift or nonurinary loss).
  - Spot urine potassium to creatinine ratio: if more than 13 meq/g (1.5 mEq/mmol) of creatinine indicates inappropriate urinary loss.
- Asses acid base status:
  - Metabolic acidosis with low urinary excretion of potassium is due to lower gastrointestinal loss like diarrhea.
  - Metabolic acidosis with high urinary potassium excretion is due to diabetic ketoacidosis or type 1 renal tubular acidosis.
  - Metabolic alkalosis with low urinary excretion of potassium is due to upper gastrointestinal loss like vomiting or previous diuretic use.
  - Metabolic alkalosis with high potassium urinary loss is due to recent diuretic use or primary hyperldosteronism.

Step 7: Send Investigation

- Complete blood count.
- Na, K, Ca, Mg, PO_4, HCO_3.
- Urea, creatinine.
- Creatine phosphokinase (CPK) (to exclude hypokalemia-induced rhabdomyolysis).
- Arterial blood gas analysis is performed to ascertain pH.
- ECG.
- Urine for K, creatinine.
- Urinalysis.

Step 8: Replace Potassium Orally

- Once serum potassium has been raised to a safe limit of above 3 mEq/L, the rest of the replacement may be done slowly by oral route. This could be achieved by adding a potassium-rich diet, potassium salt, or potassium chloride suspension.
- Treatment usually starts with 10–20 mEq of potassium chloride given 2–4 times per day (20–80 mEq/day).
- Potassium bicarbonate orally is preferred in patients with hypokalemia and metabolic acidosis.
- Potassium phosphate should be considered as replacement in patients with concomitant hypophosphotemia due to refeeding syndrome or proximal renal tubular acidosis.

Step 9: Reduce the Loss of Potassium

- In patients with hypokalemia due to increased urinary losses, potassium-sparing diuretics such as spironolactone, amiloride, or eplerenone may be tried.
- Spironolactone or eplerenone is the drug of choice for hypokalemia due to primary hyperaldosteronism.
- Oral/IV potassium should be used with caution in these situations, especially in patients with impaired renal function and on concomitant use of ACE inhibitors or ARBs.

Hyperkalemia

A 60-year-old diabetic male patient, hypertensive and on angiotensin-converting enzyme (ACE) inhibitors, was admitted with dizzy spells. On admission, his pulse was 60/min, BP was 110/70 mmHg, and sensorium was normal. His blood biochemistry showed urea 90 mg/dL, creatinine 2.0 mg/dL, Na 130 mEq/L, and K 6.5 mEq/L.

Step 1: Initiate Resuscitation

- Patients with severe hyperkalemia need an urgent intravenous access and continuous ECG monitoring.
- They can have sudden bradycardic arrest. ACLS protocol should be followed in these situations (see Chap. 19, Vol. 1).
- Intravenous calcium gluconate/chloride should be immediately given in cardiac arrest situations when hyperkalemia is suspected, even before potassium results are available.
- Avoid succinylcholine in suspected hyperkalemia during rapid sequence intubation.
- Avoid potassium-containing resuscitation fluid like Ringers lactate and balanced salt solution during resuscitation.

Step 2: Assess the Severity of Hyperkalemia and Urgency of Correction

- Hyperkalemia should be urgently managed in the following circumstances:
  - ECG changes (see Table 3.4 and Fig. 3.2).
  - The progression and severity of ECG changes do not always corelate well with serum potassium.
- Muscle weakness or paralysis.
- Rhabdomyolysis.

Table 3.4 ECG changes in hyperkalemia

Tall, peaked T waves with a shortened QT interval
Progressive lengthening of the PR interval and QRS duration
Disappearance of P waves
QRS widening and a sine wave pattern
Asystole and a flat ECG
Other conduction abnormalities: Right bundle branch block, left bundle branch block, bifascicular block, and advanced atrioventricular block

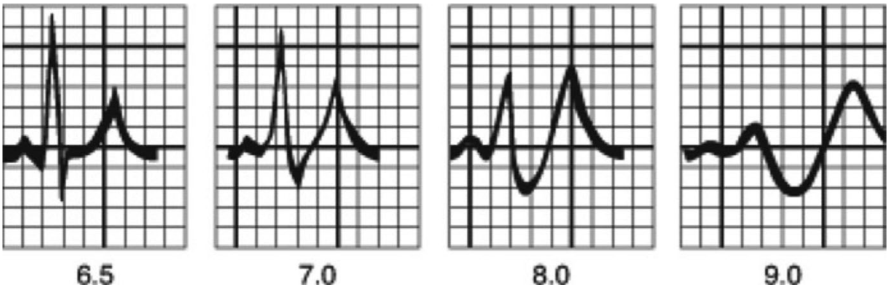

Fig. 3.2 Hyperkalemia

- Crush injury.
- Tumor lysis syndrome.
- Serum potassium of more than 7.0 mEq/L.
- Rapidly rising potassium above 5 mEq/L.
- Hyperkalemia with renal impairment and ongoing catabolic state.

Step 3: Rapidly Correct Severe Hyperkalemia

- *Intravenous calcium.*
  - Give calcium gluconate or calcium chloride—10 mL of 10% solution over 2 min under continuous ECG monitoring.
  - Intravenous calcium works within minutes, but effect is short-lasting (30–60 min).
  - Calcium acts by directly antagonizing the membrane action of hyperkalemia and does not cause lowering of serum potassium.
  - Calcium chloride contains three times more elemental calcium compared to calcium gluconate (13.6 vs. 4.6 mEq in 10 mL of 10% solution) and is the preferred drug.
  - Intravenous calcium can be repeated after 5 min if ECG abnormalities persist.
  - Concentrated calcium solution is tissue-irritant and should be given in a large peripheral vein or central vein.
  - Calcium should not be given in a bicarbonate-containing solution to avoid precipitation of calcium carbonate.

    - Calcium should be given cautiously as a slow infusion in patients on digitalis.
    - Calcium is preferably given for cases of hyperkalemia with concomitant ECG changes, but it may be given for K > 6.5 even in the absence of ECG changes.
- *Insulin with glucose.*
  - Give 10 units of regular bolus insulin intravenously along with 50 mL of 50% dextrose.
  - Monitor blood glucose every 30 min.
  - In patients with baseline hyperglycemia above 250 mg/dL, only insulin can be given.
  - The effect of insulin begins within 10 min and lasts for 4–6 h.
  - Insulin and glucose lowers serum potassium by driving potassium inside the cells.
  - It decreases serum potassium by 0.5–1.2 mEq/L.
  - Monitor capillary sugar hourly.
  - Beware of hypoglycemia in renal failure.
- *Salbutamol (albuterol) nebulizer.*
  - 10 mg in 4 mL of saline to be nebulized over 10 min (four times the usual bronchodilator dose) is given.
  - Its effect is seen within 90 min of nebulization.
  - Serum potassium usually decreases by 0.5–1.2 mEq/L.
  - It works by driving potassium inside the cell.
- *Sodium bicarbonate.*
  - It should be given cautiously in selected cases of hyperkalemia associated with severe metabolic acidosis.
  - Usual dose is 25 mEq (25 mL of 8.4%) infused over 5 min.
  - Intravenous loop diuretics: in patients with normal or mildly impaired renal function, thiazide diuretics may also be tried.

Step 4: Assess the Cause of Hyperkalemia

- Detailed history and physical examination should be performed to look for features of diseases associated with hyperkalemia such as renal failure and adrenal disease.
- History of renal disease or previous potassium levels should be looked for to assess the sudden deterioration in renal function.
- Drug history should be taken to exclude drugs such as angiotensin-receptor blockers, ACE inhibitors, nonsteroidal anti-inflammatory drugs, aldosterone antagonist, and potassium-containing drugs that can cause hyperkalemia, especially in renally impaired patients.

Step 5: Send Investigations

- Serum potassium should be monitored frequently.
- Blood urea, creatinine.
- Sodium, calcium, magnesium, phosphate.
- Arterial blood gases for pH.
- Complete hemogram.
- Blood glucose.
- CPK.
- Lactate dehydrogenase.
- Measurement of urinary potassium excretion and transtubular estimation of potassium gradient (TTKG) is of limited use in deciding the cause of hyperkalemia.

Step 6: Stop the Intake of Potassium

- Start potassium-free diet.
- Avoid the use of drugs containing potassium.
- Avoid drugs that can cause hyperkalemia.

Step 7: Remove Potassium

- *Diuretics*: A trial of loop diuretics in patients with preserved renal function and volume overload state may be done.
- *Cation exchange resin*: Sodium polystyrene sulfonate.
  - In the gut, sodium polystyrene sulfonate takes up potassium (and calcium and magnesium to lesser degrees) and releases sodium (1 gm binds to 1 mEq of potassium).
  - It is usually given orally three times daily but may be given rectally.
  - Oral dose is usually 20 g given with 100 mL of a 20% sorbitol solution to prevent constipation.
  - A major concern with sodium polystyrene sulfonate in sorbitol is the development of intestinal necrosis, usually involving the colon and the ileum.

    The serum potassium falls by at least 0.4 mEq/L in the first 24 h.

    Patiromer or sodium zirconium cyclosilicate has also been approved as a gastrointestinal potassium exchanger.
- *Dialysis.*
  - It is indicated if hyperkalemia persists in spite of the above measures or patients have any other indication of dialysis. Hemodialysis can remove 25–50 mEq of potassium per hour, with variability based on the initial serum

potassium concentration, the type and surface area of the dialyzer used, the blood flow rate, the dialysate flow rate, the duration of dialysis, and the potassium concentration of the dialysate.

- Intermittent hemodialysis is preferable than slow extended dialysis (SLED) or continuous renal replacement therapy (CRRT) for immediate decrease of severe hyperkalemia.
- Beware of rebound hyperkalemia after dialysis.

Step 8: Ascertain the Cause of Hyperkalemia and Manage Specifically (See Table 3.5)

Table 3.5 Causes of hyperkalemia

Increased potassium release from cells
Pseudohyperkalemia (hemolytic sample, marked leukocytosis, thrombocytosis, vigorous fist clenching during phlebotomy): Suspect when no ECG changes in patients with moderate to severe hyperkalemia
Metabolic acidosis
Insulin deficiency, hyperglycemia, and hyperosmolality [diabetic ketoacidosis (DKA), hyperglycemic hyperosmolar state (HHS), octreotide infusion]
Increased tissue catabolism
β-Adrenergic blockade
Rhabdomyolysis
Digitalis overdose
Hyperkalemic periodic paralysis
Succinylcholine
Tumor lysis syndrome
Severe exercise
Reduced urinary potassium excretion
Renal failure
Hypoaldosteronism [drugs (spironolactone, eplerenone, propranolol, labetalol, ARB, ACEI, NSAIDs), diabetes, adrenal insufficiency]
Hyperkalemic type 4 renal tubular acidosis
Ureterojejunostomy
Increased potassium intake (oral or intravenous, especially in patients with renal failure)

Suggested Reading

Ahee P, Crowe AV. The management of hyperkalaemia in the emergency department. J Accid Emerg Med. 2000;17:188. *A review article of hyperkalemia in the emergency department*

Clase CM, Carrero JJ, Ellison DH, et al. Potassium homeostasis and management of dyskalemia in kidney diseases: conclusions from a Kidney Disease: Improving Global Outcomes (KDIGO) Controversies Conference. Kidney Int. 2020;97:42. Consensus statement

Effa E, et al. Pharmacological interventions for the management of acute hyperkalaemia in adults. Nephrology (Carlton). 2017;22(1):5–6. *A comprehensive current review article on management of hyperkalemia*

Gennari FJ. Hypokalemia. N Engl J Med. 1998;339:451. *A review article*

Gupta AA, Self M, Mueller M, et al. Dispelling myths and misconceptions about the treatment of acute hyperkalemia. Am J Emerg Med. 2022;52:85.

McGowan CE, Saha S, Chu G, et al. Intestinal necrosis due to sodium polystyrene sulfonate (Kayexalate) in sorbitol. South Med J. 2009;102:493. *Systematic reviewed to identify all gastrointestinal specimens reported as containing SPS crystals. Patient demographics, medical comorbidities, and hospital courses of histologically verified cases of intestinal necrosis were extracted from the medical records*

Palaka E, et al. Evidence in support of hyperkalaemia management strategies: a systematic literature review. Int J Clin Pract. 2018;72(2) https://doi.org/10.1111/ijcp.13052. *A comprehensive systematic review of clinical data on management of hyperkalaemia in adults. Quantitatively comparing randomised controlled trial (RCT) data on the novel treatment sodium zirconium cyclosilicate (ZS) and established pharmacological treatments for the non-emergency management of hyperkalaemia, such as the cation-exchangers sodium/calcium polystyrene sulphonate (SPS/CPS)*

Rafique Z, Liu M, Staggers KA, et al. Patiromer for treatment of hyperkalemia in the emergency department: a pilot study. Acad Emerg Med. 2020;27:54.

Ravn Jacobsen M, Jabbari R, Glinge C, et al. Potassium disturbances and risk of ventricular fibrillation among patients with ST-segment-elevation myocardial infarction. J Am Heart Assoc. 2020;9:e014160. *A registry study*

Rossignol P, Pitt B. Sodium polystyrene is unsafe and should not be prescribed for the treatment of hyperkalaemia: primum non nocere! Clin Kidney J. 2023;16:1221.

Skogestad J, Aronsen JM. Hypokalemia-induced arrhythmias and heart failure: new insights and implivcations for therapy. Front Physiol. 2018;9:1500. *This article review the current hypokalemia-induced arrhythmias mechanism and discuss how molecular changes in heart failure might lower the threshold for these arrhythmias. They also discuss how hypokalemia-induced arrhythmias could have implications for future antiarrhythmic treatment strategies*

Website

http://www.education.science-thi.org/edu_ecg/ecginclinicalpractice/abnormalecg/potassium.html

Calcium, Phosphorus, and Magnesium Abnormalities in the ICU

4

Praveen Kumar Jain, Aditi Jain, and Ankit Jain

Case 1:
A 45-year-old man, weighing 50 kg, was admitted for intestinal perforation sepsis and acute respiratory distress syndrome (ARDS). After 10 days on the ventilator and antibiotics, he was weaned off the ventilator and started on parenteral nutrition (TPN) at 2500 kcal/day. The next day he developed difficulty in breathing, requiring reintubation and ventilator support. On investigation, S. Na 138 mEq/L, S. K 2.1 mEq/L, S. Cl 98 mEq/L, S. Ca (total) 7.2 mg/dL, S. phosphorus 0.7 mg/dL, S. Mg 1.1 mg/dL, pH 7.30, PCO2 56 mmHg, and HCO3 23 mEq/L.

Case 2:
A 75-year-old diabetic and hypertensive man was admitted in a confused state. His family noticed that for a few months he had started complaining of constipation and frequent urination even getting up few times at night. His family thought he was developing senile brain changes but brought him to

(continued)

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hospital as symptoms were deteriorating. Blood reports showed normal CBC, S. total calcium 16.7 mg/dL, S. Mg 2.0 mg/dL, S. phosphorus 3.9 mg/dL, S. albumin 3.6 g/dL, and serum PTH was suppressed. Bone marrow was negative for multiple myeloma. CT brain and cerebrospinal fluid (CSF) were normal. Ultrasound sonography (USG) abdomen and CT chest were normal. Blood tumor markers were negative.

Disorders of calcium, phosphorus, and magnesium are very common in clinical practice, yet they are often under-recognized. These minerals are vital for intracellular and hormonal functioning, and disturbances can be life-threatening.

Hypocalcemia

There are many causes for hypocalcemia (Table 4.1). The signs and symptoms of hypocalcemia can range from asymptomatic to severe life-threatening seizures, heart failure, or laryngeal spasm. Acute presentations include tetany (perioral numbness, hand and feet paresthesia, and muscular cramps), carpal spasm, and focal/generalized seizures. Physical findings are Trousseau's sign[1] and Chvostek's sign.

Table 4.1 Causes of hypocalcemia

A. Hypocalcemia with low PTH (hypoparathyroidism)
(a) Post-surgical: thyroid/parathyroid resection, radical neck dissection
(b) Post-radiation parathyroid destruction
(c) Magnesium depletion
(d) Hungry bone syndrome
(e) Infiltration of parathyroid (sarcoidosis, iron overload, metastasis)
(f) Autoimmune causes
(g) Genetic disorders
B. Hypocalcemia with high PTH (secondary hyperparathyroidism following hypocalcemia)
(a) Vitamin D deficiency or resistance
(b) PTH resistance (pseudohypoparathyroidism, hypomagnesemia)
(c) Kidney disorders
(d) Loss of circulating calcium
(i) Acute respiratory alkalosis
(ii) Acute pancreatitis
(iii) Tumor lysis
(iv) Hyperphosphatemia
(v) Osteoblastic metastasis
(vi) Critical illness, e.g., sepsis
C. Drug-induced hypocalcemia
(a) Inhibitors of bone resorption (calcitonin, bisphosphonates, denosumab)
(b) Calcium chelators: EDTA, citrate, phosphate
(c) Cinacalcet
(d) Phenytoin
D. Hypomagnesemia: (reduces PTH secretion/PTH resistance)

Approach to Hypocalcemia

Step 1: Begin Immediate Treatment If the Degree of Hypocalcemia and Rapidity of Onset Suggests Urgency to Treat

If symptoms are severe (carpal spasm, tetany, or seizures) or if complications are present (congestive heart failure or prolonged QTc interval on ECG) or corrected S. Ca < 7.5 mg/dL (1.9 mmol/L) or S. iCa < 0.8 mmol/L, treatment should not be delayed due to laboratory confirmation.

Step 2: If No Urgency to Treat, Then Confirm the Hypocalcemia

This can be done by repeating fresh measurements in the laboratory.

When dealing with total serum calcium, we must ensure to measure the serum albumin as well, as we need to correct the total serum calcium for hypoalbuminemia.

Calculate corrected total calcium for the hypoalbuminemia using correction formula:

$$\text{Corrected S. Ca} = \text{S. Ca (mg/dL)} + 0.8 \times [4 - \text{patients S. Albumin (g/dL)}]$$

For example, if the measured S. Ca is 7.5 mg/dL and S. albumin is 2 g/dL, then

$$\text{Corrected S. Ca} = 7.5 + 0.8 \times (4\text{–}2) = 9.1 \text{ mg/dL (normal)}$$

Please note that the formula for corrected calcium is an estimation and may not be accurate in all clinical scenarios. Its accuracy is poor in critically ill patients and those with advanced chronic kidney disease. In the presence of hypoalbuminemia or when the diagnosis of hypocalcemia is in doubt or symptoms are minimal or absent, measure ionized calcium (S. iCa) from a reliable laboratory.

Step 3: Compare with Old Reports

The chronicity can be established by comparing with old reports, if available.

Step 4: Once the Situation Is Non-life-threatening, Proceed to Establish an Etiology

1. The etiology may be clinically obvious from history or examination.
   (a) History of hypocalcemia in the family suggests a genetic cause.
   (b) History of thyroid/parathyroid surgery or radical neck dissection (or neck scar) suggests postsurgical damage.
   (c) Presence of mucocutaneous candidiasis and adrenal insufficiency suggests polyglandular syndrome and hence autoimmune parathyroid destruction.

Table 4.2 Interpretation of PTH levels in a patient with confirmed hypocalcemia

PTH	S. PO4	S. Mg	25(OH) D	1,25(OH)2D	Etiology
Low/N	↑	N	N	N/low	Hypoparathyroidism Activating mutation CaSR
Low/N	N	↓/N*	N	N	Hypomagnesemia
Elevated	Low/ N	N	Low	High/N/low	Vitamin D deficiency
Elevated	↑	N	N	N/low	PTH resistance
Elevated	↑	↑/N	N	Low	Chronic kidney disease

CaSR calcium sensing receptor

   (d) Drug history: certain drugs can cause hypocalcemia (see Table 4.1).
   (e) Presence of diseases known to be associated with hypocalcemia:
      (i) Acute/chronic kidney disease
      (ii) Acute pancreatitis
      (iii) Tumor lysis syndrome/rhabdomyolysis

2. *Measure intact PT*H in all patients with hypocalcemia.
   (a) *PTH elevated:*
      (i) Consider vitamin D deficiency, renal disease (acute/chronic) or pseudohypoparathyroidism.
   (b) *PTH normal or low:*
      (i) Consider hypoparathyroidism or hypomagnesemia.
      (ii) Send for S. magnesium and treat if strongly suspected (as Mg is an intracellular ion and serum levels do not correlate with the actual state of Mg deficiency). Hypocalcemia should resolve within minutes or hours of magnesium correction if hypomagnesemia is the cause.
      (iii) A serum PTH within the normal range in a patient with hypocalcemia is inappropriately normal/low.
3. *Other useful investigations* are S. phosphates, S. magnesium, 25-hydroxy vitamin D, 1–25 dihydroxy vitamin D, S. amylase, and S. creatinine. For interpretation, see Table 4.2.

Step 5: Begin Appropriate Treatment

The treatment of hypocalcemia varies with its severity and the underlying cause.

1. *Symptomatic acute severe hypocalcemia or asymptomatic patients with corrected (for albumin) S. Ca ≤ 7.5 mg/dL (≤1.9 mmol/L) or S. iCa ≤ 3 mg/dL (≤0.8 mmol/L):*
   (a) Treat with IV 10% solution of Ca-gluconate (90 mg elemental calcium per 10 mL). A solution of 1000 mg elemental calcium is diluted with NS or D5W to make a total 1 L solution and infused at 50 mL/h.
   (b) Most patients require 0.5–1.5 mg elemental calcium/h replacement. Simultaneously, treat the cause, e.g., oral calcium (1–4 gm/day of elemental calcium) and calcitriol (0.25–0.5 mcg twice a day) for acute hypoparathyroidism.

   (c) If coexisting hypomagnesemia or resistant hypocalcemia despite the above treatment: replace Mg as IV MgSO4 (4–8 gm/day as slow infusion over 10–12 h in the absence of renal failure).
2. *Mildly symptomatic or mild hypocalcemia:*
   (a) Treat with 1–2 gm of elemental calcium (calcium carbonate or citrate) given orally.
   (b) If poor or no response to oral supplementation, IV replacement can be considered.
   (c) In addition to calcium replacement, oral calcitriol is recommended.

Hypercalcemia

Hypercalcemia is a relatively common finding. Most cases (> 90%) of hypercalcemia are due to primary hyperparathyroidism and malignancy. It is easy to differentiate between these two causes as malignancy is usually evident clinically, serum calcium levels are higher, and patients are more symptomatic.

Approach to Hypercalcemia

Step 1: Begin Immediate Treatment

Begin treatment immediately if the degree of hypercalcemia and rapidity of onset suggests urgency to treat.

Step 2: Confirm the Hypercalcemia

Hypercalcemia is confirmed by repeating fresh measurements in the laboratory.

Step 3: Compare with Old Reports

Compare with old reports if available. Chronic and asymptomatic hypercalcemia is highly suggestive of primary hyperparathyroidism.

Step 4: Calculate Corrected S. Ca Corrected for S. Albumin

In patients with hypoalbuminemia, the hypercalcemia may be underestimated, while in hyperalbuminemia, it may be overestimated (pseudohypercalcemia). A similar situation may occur in multiple myeloma where calcium binds with abnormal globulin rather than albumin. (See step 2C under hypocalcemia for calculations and formula).

Table 4.3 Causes of hypercalcemia

A. Parathyroid related:
(a) Primary hyperparathyroidism
(b) Tertiary hyperparathyroidism (renal failure)
(c) Familial hypocalciuric hypercalcemia
B. Non-parathyroid related:
(a) Hypercalcemia of malignancy
(b) Vitamin D toxicity
(c) Chronic granulomatous diseases
C. Medications:
(a) Thiazides
(b) Lithium
(c) Teriparatide (treatment of osteoporosis)
D. Miscellaneous:
(a) Immobilization
(b) Milk alkali syndrome
(c) Endocrine disorders: hyperthyroidism, acromegaly, adrenal insufficiency, pheochromocytoma

Step 5: Determine the Etiology

A. *Look at the degree of hypercalcemia.*
   (a) Primary hyperparathyroidism: mild hypercalcemia with S. Ca < 11 mg/dL (2.75 mmol/L).
   (b) Hypercalcemia of malignancy: S. Ca > 13 mg/dL (3.25 mmol/L). If the patient is symptomatic or S. Ca > 14 mg/dL (3.5 mmol/L), begin treatment immediately.

B. *Review diet and medication history* (nonprescription/herbal/vitamin supplements). See Table 4.3.

C. *Measure serum PTH.* If the patient is asymptomatic or mildly symptomatic or S. Ca < 11 mg/dL, review serum PTH and S. calcium levels.
   (a) PTH elevated: primary hyperparathyroidism.
   (b) PTH mildly elevated: primary hyperparathyroidism or familial hypocalciuric hypercalcemia.
   (c) PTH low/normal: Non-PTH-mediated hypercalcemia-like malignancy. If malignancy not clinically obvious, do S. PTHrP, 25(OH)vitD, 1–25(OH)2VitD.
      (i) PTHrP elevated: humoral hypercalcemia of malignancy.
      (ii) PTHrP not elevated but 1–25(OH)2VitD elevated: granulomatous disease like sarcoidosis and lymphoma likely.
      (iii) PTHrP not elevated but 25(OH)VitD elevated: vitamin D toxicity.
      (iv) PTHrP not elevated and 25(OH)VitD not elevated: send serum/urine for electrophoresis: consider multiple myeloma.

Step 6: Treat the Hypercalcemia

The aim is to lower the serum calcium concentration and, if possible, correct the underlying disease.

A. *Mild hypercalcemia*: S. Ca < 12 mg/dL (3 mmol/L). Patient asymptomatic or mild symptoms. No immediate treatment is needed. Avoid factors that aggravate hypercalcemia (e.g., medications like thiazide diuretics or lithium, vitamin D/calcium supplements, prolonged inactivity, volume deletion, etc.). Ensure adequate hydration (6–8 glasses of water per day). Treat any cause identified.
B. *Moderate hypercalcemia*: S. Ca 12–14 mg/dL (3–3.5 mmol/L). If chronic, immediate treatment may not be needed unless symptomatic. Treatment with hydration (NS) and bisphosphonates. Treat the underlying cause simultaneously.
C. *Severe hypercalcemia*: S. Ca >14 mg/dL (>3.5 mmol/L) or severe symptoms such as altered sensorium and coma. Need aggressive treatment.
   (a) *IV hydration with NS* @ 200–300 mL/h adjusted to maintain urine output at 100–150 mL/h Exercise caution in the elderly, with congestive heart failure or renal impairment. Avoid using loop diuretics.
   (b) *Subcutaneous/IM calcitonin* @ 4 U/kg. Recheck S. Ca after 4–6 h. If the drop in S. calcium is seen, repeat calcitonin every 12 h for 24–48 h. If the response to the initial dose of calcitonin is poor, then increase the dose to 8 U/kg.
   (c) *Bisphosphonate* (IV zoledronic acid 4 mg IV over 15 min, dose adjustment and slow infusion of the drug is needed if S. creatinine is raised).
   (d) *Denosumab* if bisphosphonates are not effective or contraindicated (allergy, renal impairment). With creatinine >4.5 mg/dL. Dose 60 mg subcutaneous should be given. Calcium should be monitored closely in patients with renal impairment as there is a higher risk of hypocalcemia than bisphosphonate.
   (e) *Specific treatment of cause*: For example, glucocorticoids and low calcium diet for sarcoidosis/lymphoma.
   (f) *Hemodialysis* with calcium-free dialysate in refractory hypercalcemia is advised.

   Saline and calcitonin reduce S. Ca levels within 12–48 h while bisphosphonates are effective by 2–4 days and provide the more sustained effect.

Hypophosphatemia

Step 1: Exclude Pseudohypophosphatemia

Falsely low S. phosphate levels can be present due to multiple myeloma, medications, e.g., large doses of IV mannitol (interferes with lab estimation), and liposomal amphotericin.

Step 2: If True Hypophosphatemia

If S. phoshate levels are <2.5 mg/dL, then establish the cause of hypophosphatemia. See Table 4.4.

Table 4.4 Causes of hypophosphatemia

- A. *Decreased uptake (intestinal absorption):*
  - (a) Poor intake
  - (b) Chronic diarrhea and steatorrhea
  - (c) Vitamin D deficiency
  - (d) Inhibition of phosphate absorption (antacids, phosphate binders, Niacin)
- B. *Increased loss (urinary excretion/dialysis):*
  - (a) Primary/secondary hyperparathyroidism
  - (b) Vitamin D deficiency/resistance
  - (c) Hereditary hypophosphatemic rickets
  - (d) Fanconi syndrome
  - (e) Medications: acetazolamide, IV iron, chemotherapeutic agents
  - (f) Renal replacement therapies
- C. *Transcellular shift/redistribution:*
  - (a) Insulin therapy
  - (b) Refeeding syndrome
  - (c) Acute respiratory alkalosis
  - (d) Hungry bone syndrome
  - (e) Sepsis

Step 3: If Unexplained Hypophosphatemia

A. *Repeat S. phosphate estimation* in laboratory to confirm persisting hypophosphatemia. To exclude transient transcellular shift that may have corrected in 12–24 h.

B. *Review medications*: see Table 4.4.

C. *Rule out malnutrition* from diet history.

D. *Review biochemistry*: S. Ca, S. Mg, S. HCO3, BUN/creatinine, and S. glucose.
   - (a) If S. Ca is high: measure PTH for hyperparathyroidism.
   - (b) If S. Ca is low: measure vitamin D to exclude vitamin D deficiency.

E. *If etiology is still unexplained, estimate 24 h urinary phosphate excretion* or fractional excretion of filtered phosphate ($FEPO_4$) from a random urine specimen. If urinary phosphate is <100 mg/day or FEPO4 < 5%, then PO4 loss is extrarenal; on the other hand, if urinary phosphate is >100 mg/day or FEPO4 > 5%, then phosphate loss is renal in origin (Table 4.4).

Step 4: Treat the Hypophosphatemia

A. *Treat the underlying causes of hypophosphatemia.* This is usually sufficient in most cases.

B. *Phosphate replacement:*
   - (a) If S. phosphorus <2 mg/dL (0.64 mmol/L), oral replacement advisable.
   - (b) If S. phosphorus 1–1.5 mg/dL (0.48–0.64 mmol/L) or the patient is very symptomatic with muscular weakness (respiratory fatigue, ileus), encephalopathy, hemolysis, then treat with IV replacement. The dose of IV phosphate will vary from 0.2 mmol/kg to 0.4 mmol/kg over 4 h.

Table 4.5 Causes of hyperphosphatemia

A. Acute phosphate load:
(a) Endogenous: Cell cell lysis (tumor lysis syndrome, rhabdomyolysis)
(b) Exogenous
(i) Phosphate-rich medication (laxatives, fosphenytoin)
(ii) Intestinal uptake due to vitamin D toxicity
(iii) Hemolysis, transfusion of stored blood
B. Decreased renal clearance:
(a) Acute/chronic kidney disease
(b) Increased renal tubular reabsorption (bisphosphonates, vitamin D toxicity, hypoparathyroidism)
C. Transcellular shift/redistribution (into extracellular space): ketoacidosis, lactic acidosis
D. Pseudohyperphosphatemia:
(a) Endogenous: hemolysis, hyperlipidemia, multiple myeloma
(b) Exogenous: medication (heparin, amphotericin B, tissue plasminogen activator)

Hyperphosphatemia

Step 1: Determine the Reason for Hyperphosphatemia

See Table 4.5.

Step 2: Treat the Hyperphosphatemia

A. *Treatment of acute hyperphosphatemia*: If kidney function is good, simple hydration with NS is enough. If symptomatic or life threatening or kidney disease, then consider hemodialysis.

B. *Treatment of chronic hyperphosphatemia*: In patients with CKD, treat with low phosphate diet and phosphate binders.

Hypomagnesemia

Hypomagnesemia is defined as S. Mg < 1.7 mg/dL in adults. However, it must be differentiated from (intracellular) Mg deficiency, which is extremely common in patients even when the S. Mg levels are in normal range. A physician must clinically suspect intracellular hypomagnesemia under certain scenarios (see Table 4.6).

Step 1: Suspect Hypomagnesemia

Hypomagenesmia should be suspected in situations where lower S. Mg levels are extremely common. (see Table 4.6). The etiology is easily determined if any of the clinical above scenarios exist (e.g., chronic diarrhea, diuretic use, etc.).

Table 4.6 When to clinically suspect hypomagnesemia

A. Malnutrition
B. Chronic alcoholism
C. Chronic diarrhea
C. Chronic diuretic use
D. Diabetics especially poorly controlled
F. Aminoglycoside therapy
G. Refractory hypokalemia
H. Patients who develop Torsade de Pointes
I. Patients with (hypokalemia + hypocalcemia)
J. Neuromuscular disturbances such as tetany, seizures, and weakness
K. Ventricular arrythmias

Table 4.7 Causes of hypomagnesemia

A. GI loss:
(a) Diarrhea, malabsorption
(b) Acute pancreatitis
(c) Medications: proton pump inhibitors
B. Urinary losses:
(a) Medications: diuretics, aminoglycoside antibiotics, amphotericin, cisplatin
(b) Uncontrolled diabetes
(c) Chronic alcoholism
(d) Hypercalcemia
(e) Post-kidney transplant
C. Genetic disorders:
(a) Bartter syndrome
(b) Gitelman syndrome
(c) Familial hypomagnesemia

Step 2: Exclude Spurious Hypomagnesemia

This happens due to EDTA contamination of blood sample or with severe hypoalbuminemia. EDTA contamination suspected when "hypomagnesemia + hyperkalemia" or "hypomagnesemia + hypocalcemia" pattern seen in biochemistry.

Step 3: Determine the Etiology of Hypomagnesemia

The cause of the hypomagnesmia should be determined. See Table 4.7.

Step 4: If Hypomagnesemia Still Unexplained

Estimate 24 urinary Mg. 24 h urinary Mg < 10 mg/day suggests extrarenal cause. While 24 h urinary Mg >15–30 mg/day suggests renal cause.

Step 5: If Hypomagnesemia Is Severe

Does the patient have severe hypomagnesemia (S. Mg < 1 mg/dL) or severe symptoms (arrhythmias, tetany, seizures)?

A. Obtain 12 lead ECG/ monitor. If the patient is hemodynamically unstable (e.g., arrhythmias), give 1–2 gm MgSO4 over 15–20 min. Once stable, slow infusions of 6–8 gms/day are strongly recommended (given as an infusion over 8–10 h). Dose should be reduced to 50% in the presence of renal failure.
B. Treat associated metabolic abnormalities (hypokalemia, hypocalcemia, metabolic alkalosis).
C. Identify and correct the underlying causes of hypomagnesemia.
D. After the acute correction of hypomagnesemia, a dose of 6–8 gm MgSO4 is given in 500 mL saline over 10–12 h/day over a few days even after serum magnesium normalizes. This is to replenish the intracellular stores.
E. Potassium-sparing diuretics (triamterene, amiloride) or SGLT2 inhibitors may be used in patients with renal magnesium wasting and/or refractory hypomagnesemia.

Step 6: If Mild-to-moderate Hypomagnesia

Does the patient have mild-to-moderate hypomagnesemia: (S. Mg > 1 mg/dL) or is asymptomatic?

A. Identify and correct the underlying causes of hypomagnesemia.
B. If unexplained, estimate 24 h urinary magnesium to categorize as renal magnesium losing nephropathy or extrarenal loss.
C. Replace magnesium orally or IV depending on the circumstances.

Hypermagnesemia

Hypermagnesemia is an uncommon problem in the absence of large magnesium administration (e.g., eclampsia or pre-eclampsia treatment), kidney failure, or increase intestinal absorption (constipation, gastritis, colitis, gastric ulcer).

Step 1: Prevention

The dose of MgSO4 should be reduced when treating hypomagnesemia in a patient with renal failure.

Step 2: If Renal Function Is Near Normal

Stopping Mg replacement is all that is needed. Loop diuretics can be used to increase Mg excretion.

Step 3: If Renal Function Is Moderately to Severely Impaired

Stopping Mg replacement + IV normal saline + loop diuretic. If this treatment fails or patient is severely symptomatic, consider hemodialysis. In severely symptomatic patients, IV calcium (100–200 mg of elemental calcium given over 10 min) can be given as a magnesium antagonist to reverse the neurological and cardiovascular effects of hypermagnesemia.

Discussion of Case 1 (refer to the case when needed): This critically ill patient with acute intestinal perforation, sepsis, and ARDS was on only IV saline for 10 days; on the 11th day, he is weaned off successfully but also started on TPN at 50 kcal/kg (2500 kcal/day), which is higher than the recommended 25–30 kcal/kg, resulting in a classical refeeding syndrome. Severe hypophosphatemia, hypokalemia, and hypomagnesemia due to the sudden insulin release after prolonged starvation resulted in severe skeletal muscle weakness and hypoventilation. The patient had to be reintubated and ventilated. Parenteral nutrition stopped and electrolytes corrected. Thereafter, parenteral nutrition was gradually reintroduced starting at 750 kcal/day and built up. Interpretation: refeeding syndrome.

Discussion of Case 2: Upon review of the prescriptions with the family, it was seen that this elderly gentleman with osteoporosis was given injection Arachitol 6,00,000 U every 2 weeks for the past 1 year by his family physician. High S. calcium can have many causes like hyperparathyroidism, but here the S. phosphorus is not suppressed (relatively high), suggesting vitamin D toxicity or bone metastasis. There was no evidence of malignancy or metastasis to bones. Interpretation: iatrogenic hypercalcemia from vitamin D toxicity.

Suggested Reading

Adomako EA, Yu ASL. Magnesium disorders: core curriculum 2024. Am J Kidney Dis. 2024;83:803. *Review article*

Cooper MS, Gittoes NJ. Diagnosis and management of hypocalcaemia. BMJ. 2008;336:1298. *A review article*

Kraft MD, Btaiche IF, Sacks GS, Kudsk KA. Treatment of electrolyte disorders in adult patients in the intensive care unit. Am J Health Syst Pharm. 2005;62:1663.

Lafferty FW. Differential diagnosis of hypercalcemia. J Bone Miner Res. 1991;6(Suppl 2):S51.

5

Arterial Blood Gases

Sharmili Sinha, Tapas Kumar Sahoo, and K. M. Ganesh

A 38-year-old morbidly obese man presented with complaints of fever, abdominal wall tightness, and pain and was diagnosed with abdominal wall cellulitis, with acute kidney injury (AKI). Upon evaluation, his arterial blood gases and the electrolytes sample, which were simultaneously drawn, are given in Table 5.1. Evaluate the acid–base disturbance.

Arterial blood gas analysis is an essential component of diagnosing and managing critically ill patients in the ICU. The proper understanding and application of the concepts of acid–base balance will help the clinician to follow the progress of the patient and evaluate the effectiveness of the treatment provided to them.

Table 5.1 ABG and electrolytes value

pH	7.17	Na	131
PaCO2	66	K	5.9
PaO2	72	Cl	91
HCO3	18.8	Mg	1.6
SBE	−6.1	PO4	7.1
Lact.	16	Alb	3.3
		Ca	7.0

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Step 1: Take an Arterial Blood Sample

- If possible, take an arterial blood gas (ABG) sample at room air and start oxygen supplementation immediately.
- The radial artery is preferred for collecting the sample, Allen's test or modified Allen's test is done to check for patency of the ulnar arterial circulation.
- Prefer to use 22-gauge needle.
- Avoid air bubbles.
- Cool the sample immediately (if transport is necessary for analysis).

A. Potential sampling error
  - Air contamination—spurious increase in PO_2.
  - Duration of exposure is more important than the volume of air bubbles.
  - Expel air immediately.
  - Discard the sample if froth is present.

B. Venous sample—absence of flash of blood on entry into the vessel, absence of pulsations during syringe filling, and absence of auto-filling of the syringe.
  - Cross-check with pulse oximetry and clinical status.

C. Anticoagulant effects: Excess heparin can cause dilutional errors, may cause a fall in PaCO2 and HCO3, giving a false picture of metabolic acidosis and respiratory compensation. However, pH remains unchanged if nonacidic (lithium) heparin is used.

D. Metabolism: If analyzed late and kept at room temperature, blood cells consume O_2, produce CO_2, and lower pH. Spurious hypoxemia should also be kept in mind, especially if the leukocyte counts are very high as in cases of blast crisis (leucocyte larceny).

Step 2: Take a Detailed History and Do a Proper Clinical Examination

- Very often it is the presenting symptom or signs that are a clue to the interpretation of the acid–base status.
- For example, in a patient with vomiting, the primary acid–base problem could be metabolic alkalosis (due to loss of hydrochloric acid) as opposed to someone with diarrhea, whose primary problem could be metabolic acidosis (due to loss of bicarbonate ions).
- The important aspect to remember is that it is the underlying disorder of the patient that determines the acid–base status and not just the pH of the blood.
- A stepwise approach helps interpret ABG correctly.
- Interpretation of serum electrolytes is also important for an accurate estimation of mixed acid–base disorders.

Step 3: Know the Normal Values

	Normal range	For calculation
pH	7.34–7.45	7.4
PCO_2	35–45	40
HCO_3	22–26	24
PO_2	>80	>95

Step 4: Do a Validity Check of the ABG Report to Authenticate the Report

A. $H^+ = 24$´PCO_2/HCO_3

  Place the value of PCO_2 and HCO_3 and calculate H^+.

  Calculate H^+ from pH as seen on ABG:

B. Rule of thumb

  1. At pH of 7.4, H^+ concentration is 40.

    For every 0.1 ↓ in pH, multiply H^+ concentration sequentially by 1.25.

    For every 0.1 ↑ in pH, multiply H+ concentration sequentially by 0.8.

  2. 80-Last two digits of pH after decimal = H^+ (e.g., if pH 7.35, H^+ = 80–35 = 45).

C. Match the H^+ concentration by two methods: A and B.

  If it is matching, ABG is valid.

  If it does not match, recheck the ABG.

Step 5: Assess Oxygenation

- Look at oxygenation (PaO_2 and SaO_2).
- Look at the PaO_2/FiO_2 ratio.
  - Normally the ratio is around 1:400 to 1:500 given the fact that at 0.21 FiO_2 the PaO_2 is approximately 100 mmHg.
  - Less than 1:400—suggestive of V-Q mismatch or diffusion defect or intracardiac shunt.
  - Less than 300 with bilateral lung infiltrate in chest skiagram—mild acute respiratory distress syndrome (ARDS).
  - Less than 200 with bilateral lung infiltrate in chest skiagram—moderate ARDS.
  - Less than 100—severe ARDS.
  - Expected normal oxygen on room air: 100–1/3 (age).
  - Expected normal oxygen on supplemental oxygen: FiO2 (in decimals) X 500.
  - FiO2 increases by approximately 4% for each liter increase in supplemental oxygen above room air (0.21).
- A-a gradient
  - A-a gradient = $PAO_2 - PaO_2$

    PAO_2 is alveolar PO_2 (calculated from the alveolar gas equation) and PaO_2 is arterial PO_2 (measured in arterial blood) A.

  - In general, the A-a gradient can be calculated by

    A-a gradient = $[FiO2'(P_{atm}-P_{H2O})-(PaCO2/0.8)]-PaO2$

    On room air and at sea level, the FiO_2 is 0.21, the P_{atm}. is 760 mmHg, and P_{H2O} is 47 mmHg.
  - On room air, PAO_2 can be calculated by

    150–PaCO2/0.8
- Normal A-a gradient in a 20-year-old person is 5 mmHg, which increases to 10 mmHg in a 35-year–old person. If A-a gradient is 20 mmHg at any age, it is abnormal.
- Rule of thumb: A-a gradient (on room air) = 2.5 + 0.21× age in years

Step 6: Assess Acid–Base Disorder (Boston Approach)

I. Look at the pH—is there acidemia or alkalemia?

A normal pH would suggest a mixed disorder or a normal acid–base status.

II. Check CO_2 and HCO_3^- to determine whether the primary problem is metabolic or respiratory in origin.

III. If the primary disorder is respiratory, determine whether it is an acute disorder or a chronic disorder.

IV. Apply the rules of compensation to know if it is a simple or a mixed disorder.

V. Mind the gaps—anion gap, delta gap, osmolar gap, and saturation gap.

I. *Look at the pH*

The pH is actually the –log $[H^+]$. By altering either the PCO_2 or the HCO_3^-, $[H^+]$ will change, and so will pH.

- An acidemia (low pH) can result from either a low $HCO3^-$ (metabolic) or a high CO2 (respiratory).
- An alkalemia (high pH) can result from either a high $HCO3^-$ (metabolic) or a low CO2 (respiratory).
- Diiferentiate between “emia” and “osis.” For example, a person can be acedemic (pH low) but may also have metabolic alkalosis.

II. *Look at the CO_2 and HCO_3^- to determine if the primary problem is metabolic or respiratory in origin*

The primary acid–base disturbances include the following:

- Low pH: low $HCO3^-$—metabolic acidosis
- High pH: high $HCO3^-$—metabolic alkalosis
- Low pH: high PCO2—respiratory acidosis
- High pH: low PCO2—respiratory alkalosis

A1. *Metabolic acidosis*

- Metabolic acidosis results from a primary decrease in plasma $[HCO3^-]$.
- It is due to either an excretion of bicarbonate-containing fluids or by utilization of bicarbonate.
- It is very important to calculate the anion gap (AG) if the primary disorder is metabolic acidosis.

- AG = Na + −(Cl- + HCO3); the normal AG is 12 ± 2 mEq/L.
- In non-AG metabolic acidosis, the bicarbonate losses are accompanied by cation loss, hence no change in AG (Table 5.2).
- A higher gap usually denotes the presence of unmeasured anions in the body (Table 5.3).
- Remember to correct AG for hypoalbuminemia, which is very common in ICU patients. For this for every 1gm% drop in albumin below 4 gm%, add 2–3 to the calculated gap.
- Check urinary AG in non-AG metabolic acidosis (U Na + U K-U Cl)
  - Normal—zero or negative
  - Nonrenal loss of bicarbonate (diarrhea)—negative
  - Renal loss of bicarbonate or decreased H+ excretion (renal tubular acidosis)—positive

A2. *Metabolic alkalosis (high HCO_3)*

- Metabolic alkalosis reflects an increase in plasma $[HCO3^{-1}$.
- It is due to either gain of $HCO3^-$ or extracellular volume contraction.
- It can be classified into saline-responsive or nonresponsive. For this spot, urinary chloride can be checked.
- More than 20 mEq/L urinary chloride is saline unresponsive (Table 5.4) and less than 20 mEq/L urinary chloride is saline responsive (Table 5.5).

Table 5.2 Causes of a non-anion gap metabolic acidosis (HARDUP)

H	⟹ Hyperalimentation/Hyperchloremia
A	⟹ Acetazolamide/Addison's disease
R	⟹ Renal tubular acidosis
D	⟹ Diarrhea
U	⟹ Uremia-acute/Ureteroureterostomies
P	⟹ Postintubation hypocapnia/Portoenterostomies

Table 5.3 Causes of a raised anion gap metabolic acidosis (MUDPILERS)

M	⟹ Methanol
U	⟹ Uremia-chronic
D	⟹ Diabetic ketoacidosis
P	⟹ Paraldehyde
I	⟹ Isoniazid, iron
L	⟹ Lactate
E	⟹ Ethanol, ethylene glycol
R	⟹ Rhabdomyolysis/renal failure
S	⟹ Salicylate

Table 5.4 Urine Cl^- more than 20 mEq/L (usually saline unresponsive)

Primary hyperaldosteronism
Cushing's syndrome, ectopic ACTH
Exogenous steroids, licorice ingestion, tobacco chewing
Adrenal 11 or 17 OH defects
Liddle's syndrome
Bartter's syndrome
K+ and Mg2+ deficiency
Milk-alkali syndrome

Table 5.5 Urine Cl^- less than 20 mEq/L (usually saline responsive)

Vomiting, nasogastric suctioning
Chloride-wasting diarrhea
Villous adenoma of colon
Post-hypercapnia
Diuretic therapy

- The reason for using urinary chloride rather than urine sodium to ascertain volume status, as due to metabolic alkalosis serum bicarbonate is high, which is filtered, thereby confounding urine sodium value for volume status.

B. *Respiratory acidosis (high PCO_2)*
  - Respiratory acidosis is due to a primary rise in CO2.
  - Hypercapnia almost always results from alveolar hypoventilation due to one of the following causes:
  1. Respiratory center depression
  2. Neuromuscular disorders
  3. Upper airway obstruction
  4. Pulmonary disease

C. *Respiratory alkalosis (low PCO_2)*
  - A respiratory alkalosis is due to a decrease in PCO_2.
  - It results from hyperventilation leading to a decrease in CO_2.

  Causes of respiratory alkalosis
  - Hypoxemia from any cause
  - Respiratory center stimulation
  - Mechanical hyperventilation
  - Sepsis, pain, fever

III. *If the primary disorder is respiratory, determine whether it is an acute disorder or a chronic disorder*

A. You must also take into consideration the patient's history while interpreting ABG. However, the following formulae help in this.
  - Normal pH is 7.4
  - Calculate the change in pH (from 7.4)

    An acute respiratory disorder (acidosis or alkalosis)
    Change in pH = 0.008´($PaCO_2$–40)
    Expected pH = 7.4 ± change in pH

B. In chronic respiratory disorder (acidosis or alkalosis)
    Change in pH = 0.003´($PaCO_2$–40)
    Expected pH = 7.4 ± change in pH

- *Compare the pH on ABG*
  - If the pH on ABG is close to **A**, it is an acute disorder.
  - If the pH on ABG is close to **B**, it is a chronic disorder.
  - May follow rule of 1–2–3–4 (Table 5.6).
  - For each 10 mmHg rise or fall of PaCO2, HCO3 will change.
  - Acute respiratory acidosis: rise by 1.

Table 5.6 CO2and HCO$^{-}_{3}$ compensation

Primary disorder	Initial chemical change	Compensatory response	Compensatory mechanism	Expected level of compensation
Metabolic acidosis	↓ HCO_3^-	↓ PCO_2	Hyperventilation	$PCO_2 = (1.5 \times [HCO_3^-]) + 8 \pm 2$
				PCO_2 = last two digits of pH
Metabolic alkalosis	↑ HCO_3^-	↑ PCO_2	Hypoventilation	$PCO_2 = (0.7 \times [HCO_3^-]) + 21 \pm 2$
				PCO_2 = last two digits of PH
Respiratory acidosis	↑ PCO_2	↑ HCO_3^-		
Acute			Buffering—rule of 1	↑ $[HCO_3^-])]$ = 1 mEq/L for every 10 mmHg delta PCO_2
Chronic			Generation of new HCO_3^-—rule of 4	↑ $[HCO_3^-])$ = 4 mEq/L for every 10 mmHg delta PCO_2
Respiratory alkalosis	↓ PCO_2	↓ HCO_3		
Acute			Buffering—rule of 2	↓ $[HCO_3^-])$ = 2 mEq/L for every 10 mmHg delta PCO_2
Chronic			Decreased reabsorption of HCO_3^-—rule of 4	↓ $[HCO_3^-])$ = 3 mEq/L for every 10 mmHg delta PCO_2

  - Acute respiratory alkalosis: fall by 2.
  - Chronic respiratory acidosis: rise by 3.
  - Chronic respiratory alkalosis: fall by 4.

IV. *CO_2 and HCO_3^- compensatory mechanism* (Table 5.6)

V. *Mind the gaps*

A1. Calculate AG in case of metabolic acidosis.

High denotes raised AG metabolic acidosis, and normal or narrow denotes non-AG acidosis.

A2. Calculate adjusted AG.

Adjusted AG = calculated AG + 2.5′(4–Serum albumin in gm%).

B. In less obvious cases, the coexistence of two metabolic acid–base disorders may be apparent by calculating the difference between the change in AG (delta AG) and the change in serum HCO_3^- (delta CO_2). This calculation is called the bicarbonate gap or the delta gap:

- Bicarbonate (delta) gap = delta AG-delta HCO_3^-
- Where delta AG = patient's AG- 12 mEq/L{normal AG};
- Delta HCO_3^- = 24 mEq/L{normal HCO_3^-}-patient's HCO_3^-.

- Normally the delta gap is zero if there is only AG acidosis. A positive raised delta gap or a decreased delta gap denotes the presence of mixed lesion.
- A positive delta gap of more than 6 mEq/L is suggestive of presence of metabolic alkalosis and/or HCO_3^- retention.
- The delta gap of less than 6 mEq/L is suggestive of the presence of hyperchloremic acidosis and/or HCO_3^- excretion.

- *Urinary anion gap*
  - Urinary anion gap is measured to determine the source of HCO3 loss.
  - UAG = Urinary Na^+ + Urinary K^+ − Urinary Cl^-
  - Normally UAG is zero or slightly negative. During Normal AG metabolic acidosis, the kidney increases ammonia excretion in the form of NH4Cl, leading to more negative UAG, usually ranging from—20 to—50 mEq/L. This is observed in cases of HCO 3 loss due to nonrenal causes like severe diarrhea. In case of metabolic acidosis due to impaired renal function such as CKD or distal RTA, UAG remains positive.

C. *Osmolar gap*

The difference between calculated plasma osmolality and the measured osmolality is called the osmolar gap. Normally the gap is less than 20 mOsm/Kg H_2O. If it is raised then it denotes the presence of unaccounted ions.

Causes of increased osmolar gap

- Ethanol
- Isopropyl alcohol
- Methanol, glycine, glycerol
- Ethylene glycol

D. *Saturation gap*

In cases of meth-hemoglobinemia, sulf-hemoglobinuria and carboxy-hemoglobinemia, in spite of high PO2 in ABG samples, the SPO2 will be low or constant in these patients. Appropriate history and exposure to certain drugs can help clinch the diagnosis.

Step 7: Look for Alerts to Mixed Acid–Base Disturbances

- Absence of compensation
- Long-standing pulmonary or renal disease
- Excessive compensation
- Respiratory assistance
- Temporal inconsistencies
- Settings conducive to mixed disturbances

Stewart's Approach of ABG Interpretation

Why Stewart's Approach?

Limitations of the traditional approach of ABG interpretation:

1. It considers HCO3 as an independent component, but HCO3 concentration can be affected by respiratory (CO2) or metabolic (H+) components, so its not a specific marker of either

$$H2O + CO2 \longleftrightarrow H2CO3 \longleftrightarrow H + +HCO3 -$$

The relationship between metabolic acidosis and HCO3 is neither consistent nor linear

2. It does not quantify metabolic component; it is indirectly calculated.
3. It does not consider the contribution of weak acids.
   - Stewart's approach puts water dissociation at the center of the acid–base status of body fluids and is modified by PCO2 and other weak acids and certain electrolytes.
   - Principles of Stewart's approach
1. Electrochemical dissociation of water determines PH

$$H2O \rightarrow H^{+} + OH^{-}$$

2. Law of mass conservation

$$[H+]^{*}\left[OH^{-}\right] = \text{Constant}$$

3. Principle of electro neutrality

$$[\text{cation}] = [\text{Anions}]^{(5)}$$

4. Independent variables determine the dissociation of water and consequently the hydrogen ion concentration to maintain electrical neutrality.
   1. *SID*

      is the difference between strong cations and strong anions, and indicates the net ionic charge of weak anions.

      Apparent SID (SID $_a$)- is the difference between measured strong cations and strong anions.

$$\text{SIDa} = \{[\text{Na}]+[\text{K}]+[\text{Ca}]+[\text{Mg}]\} - [\text{Cl}]$$

SID calculated for electroneutrality is viewed as effective SIDe and is calculated as the sum of bicarbonate and weak acids [A], albumin, and phosphate.

$$\text{SIDe} = [\text{HCO}_3] + [\text{Alb}] + [\text{Pi}]$$

[Alb]=2.8 * Alb g/dL
[Pi]=0.6 * Phosphate mg/dL
Normal range = 39+/−1.

A. SIG or unmeasured anions: By the law of electroneutrality, SID a and SIG e should be equal, but the inability to measure all strong and weak ions in the body leads to a gap between both them.

$$\text{SIG} = \text{SIDa} - \text{SIDe}$$

B. Is gap between unmeasured anions and unmeasured cations, normal range is 8 +/− 2.

2. *Weak acid total concentration (Atot)*

   It represents all nonbicarbonate buffers, that is, the total plasma concentration of weak nonvolatile acids, mainly serum albumin and phosphate. Increase in Atot is suggestive of metabolic acidosis and decrease is suggestive of metabolic alkalosis.
3. *PCO2*

   So, by law of electro neutrality:

$$\{[\mathrm{Na}]+[\mathrm{K}]+[\mathrm{Ca}]+[\mathrm{Mg}]\}=\{[\mathrm{Cl}]+[\mathrm{HCO}_3]+[\mathrm{Alb}]+[\mathrm{Pi}]+\mathrm{SIG}\}$$

Change in acid–base status occurs by either respiratory or metabolic mechanisms.

Respiratory: Change in PCO2 produces changes in PH.

$$\mathrm{CO2}+\mathrm{H2O}\longleftrightarrow\mathrm{H2CO3}\longleftrightarrow\mathrm{HCO3}+\mathrm{H}$$

Metabolic or nonrespiratory

Metabolic acid–base disturbances cannot be viewed as a consequence of a change in HCO3 as HCO3 is the dependent variable. Metabolic acid–base disorders occur due to disturbance in either SID or Atot.

A. *Changes in SID*

   Changes in SID occur by two different mechanisms:
   1. *Change in concentration*

      Change in status of hydration alters PH. Normal body PH is alkalotic, so dehydration leads to increased concentration of alkali; more alkalinity; contraction alkalosis and increase in SID; on the other hand, over hydration leads to dilution of state of alkalinity; dilutional acidosis and decrease in SID.
   2. *Change in strong ion concentration*

      Even with normal Na concentration changes in other strong ion concentration leads to alteration in SID.
      (a) *Inorganic acids*: Only strong ion capable of bringing significant change in PH is chloride. Increase in Cl concentration leads to a decrease in SID and thus acidosis and vice versa. Because Cl is measured, it leads to non-anion gap metabolic acidosis.
      (b) *Organic acids:* Increase in the concentration of one of the organic acids like lactate or keto acids leads to metabolic acidosis with high anion gap because of the presence of “unmeasured” organic acids. Chloride concentration remains normal.

B. *Change in Atot*

Atot represents nonvolatile weak acids like phosphate, albumin, and other plasma proteins. Albumin can bring significant change in acid–base status. Albumin being weak acid hypoalbuminemia leads to base excess.

Phosphate levels are normally too low to bring change in acid–base status, but in the setting of renal failure high phosphate levels leads to acidosis.

Classification of acid–base disorders

Acidosis	Alkalosis	
Respiratory	High pCO^2	Low pCO^2
Metabolic		
1. Abnormal SID		
A. Water excess/deficit	Low SID	High SID
	Low Na	High Na
B. Imbalance of strong anions		
(a) Cl excess/deficit	Low SID	High SID
	High Cl	Low Cl
(b) Unidentified anion excess	Low SID	High XA/SIG
2. Nonvolatile weak acids		
A. Serum albumin	High Alb	Low Alb
B. Phosphate	High Pi	Low Pi

Stewart's algorithm of interpretation of acid–base disorder

- Check the history and determine expected acid–base disorder.
- Collect the following data:

$$\mathrm{Na, K, Cl, Alb, PCO22, HCO3}$$

- Calculate corrected Cl for the assessment of volume status

$$\textbf{Corrected Cl} = \textbf{Observed Cl}^{*}\left(\textbf{Normal Na / Observed Na}\right)$$

Normal Na = 142
Normal range of corrected Cl = 106 +/– 2

- Calculate SID a

$$\textbf{SIDa} = \left[\textbf{Na} + \textbf{K} + \textbf{6}\right] — \textbf{Cl;}$$

(6 = value for presentation of Ca and Mg, provided they are normal)

- Calculate SIDe

$$\textbf{SIDe} = \textbf{HCO3} + \textbf{2.8}^{*}\,\textbf{Alb in g / dL} + \textbf{2}$$

(2 = substitute for Pi)

- Calculate SIG or unmeasured anions (XA)

$$\mathbf{SIG = SIDa - SIDe}$$

- Make a comparison for calculated data to its reference range.

Simplified Stewart's approach:

- Na-Cl > 40 metabolic alkalosis, <40 metabolic acidosis.
- The difference between Na and Cl needs to be explained by bicarbonate, albumin, and phosphate.
- For example, normal Na-Cl = 40, (Hco3 25 + 112(albuminX3) + 3 (Phosphate).
- If the Na-Cl gap cannot be explained, there are unmeasured anions like lactate, creatinine, and ketones.

Interpretation of ABG using standard base excess (SBE) (Copenhagen method) (Table 5.7)

The base excess approach is based on the change in metabolic acid–base change provided by the machine. The term base excess is used in clinical practice, but the machines calculate it as standard base excess (SBE), also called base excess of extracellular fluid (BE $_{ECF}$) or base excess of blood (BE$_B$). The base deficit is the negative version of base excess and is calculated as −1 X SBE.

A three-step approach is applicable when evaluating the acid–base status of a patient.

1. Evaluate the SBE in relation to pH and PCO2.
   Reference values pH 7.4, PCO2 40 mmHg, and SBE 0+- 2 mmol/L.

Table 5.7 Interpretation of ABG using standard base excess

Condition	Secondary response	Secondary response
Acute respiratory acidosis (pH decreased, $PaCO_2$ increased, SBE = 0 ± 2 mmol/L)	SBE = 0 ± 2 mmol/L	Increase of 1 mmol/L in HCO $^-$ for each 10 mm Hg increase 3 in $PaCO_2$ above 40 mm Hg
Acute respiratory alkalosis (pH increased, $PaCO_2$ decreased, SBE = 0 ± 2 mmol/L)	SBE = 0 ± 2 mmol/L	Decrease of 2 mmol/L in HCO $^-$ for each 10 mm Hg decrease 3 in $PaCO_2$ below 40 mm Hg
Chronic respiratory acidosis (pH decreased, $PaCO_2$ increased, SBE increased)	SBE = 0.4 × ($PaCO_2$_40)	Increase of 4–5 mmol/L in HCO $^-$ for each 10 mm Hg increase 3 in $PaCO_2$ above 40 mm Hg
Chronic respiratory alkalosis (pH increased, $PaCO_2$ decreased, SBE decreased)	SBE = 0.4 × ($PaCO_2$_40)	Decrease of 4–5 mmol/L in HCO $^-$ for each 10 mm Hg 3 decrease in $PaCO_2$ below 40 mm Hg
Metabolic acidosis (pH decreased, $PaCO_2$ decreased, SBE decreased)	$\Delta PaCO_2$ = SBE	Expected $PaCO_2$ = 1.5 × [HCO $^-$] + 8 ± 2 mm Hg 3
Metabolic alkalosis (pH increased, $PaCO_2$ increased, SBE increased)	$\Delta PaCO_2$ = 0.6 × SBE	Expected $PaCO_2$ = 0.7 × ([HCO $^-$] − 24) + 40 ± 2 mm Hg

2. Determine the secondary response.
   Consider mixed acid–base disorders if the secondary response differs from the expected range.
3. Evaluate the anion gap and delta gap to identify additional disorders in cases of mixed acid–base disorders.

Coming Back to Our Case

By using the six-step approach (Boston Approach)

1. Acidemia
2. Primary disorder is respiratory.
3. It is acute respiratory acidosis, as expected pH is 7.19.
4. Compensation will be metabolic alkalosis, expected HCO3 would be 26.6, and the patient's bicarb is 18.
5. Anion gap = 22 (HAGMA).
6. Delta gap = 10, delta HCO_3 = 4 (associated metabolic alkalosis).
7. Final diagnosis acute respiratory acidosis with high anion gap metabolic acidosis and metabolic alkalosis.

By using Stewart's approach

1. Corrected Cl = 98
2. SID a = 47
3. SID e = 26
4. SIG =21
5. PCO2 66
6. Final diagnosis respiratory acidosis with high anion gap metabolic acidosis and metabolic alkalosis.

By using the SBE approach

1. Respiratory acidosis
2. Secondary response will be metabolic alkalosis, expected SBE 2, in this patient it is 6, which signifies an underlying chronic respiratory acidosis (?OSA secondary to morbid obesity).
3. AG is high, delta gap 10, and delta HCO3 4.
4. Final diagnosis chronic respiratory acidosis with high anion gap acidosis and metabolic alkalosis.

Suggested Reading

Berend K. Diagnostic use of base excess in acid base disorders. N Eng J Med. 2018;378:1419–28. https://doi.org/10.1056/NEJMra1711860. *This review article provides a detail approach to acid base disorders by use of base excess*

Fencl V, Jabor A, Kazda A, et al. Diagnosis of metabolic acid-base disturbances in critically ill patients. Am J Resp Crit Care Med. 2000;162:2246–51. *Comprehensive description of acid–base disorder*

Fenwick R. Venous and arterial blood gases in respiratory failure. Emerg Nurse. 2016;24(3):26–8. *This a case-based discussion and literature review. An evidence-based approach to selecting the most appropriate test for each patient is discussed, aiming to minimize the need for unnecessary arterial sampling*

Ghosh AK. Diagnosing acid–base disorders. J Assoc Physicians India. 2006;54:720–4. *The article provides a stepwise approach for evaluation of acid–base disorder*

Kellum JA. Clinical review: reunification of acid–base physiology. Crit Care. 2005;9:500–7. *It has been emphasized that both quantitative and traditional approaches can be combined for bedside assessment of acid–base status*

Story DA, Morimatsu H, Below R. Strong ions, weak acids and base excess: a simplified Fencl-Stewart approach to clinical acid-base disorders. Br J Anaesth. 2004;92:54–60. *This article provides a simplified equation for calculation of sodium chloride effect and albumin effect on base excess*

Toffaletti JG, Rackley CR. Monitoring oxygen status. Adv Clin Chem, *This chapter reviews the causes of hypoxemia and illustrates how the oxygen parameters are used clinically in the diagnosis and management of patients with abnormal oxygenation and two clinical cases are described.* 2016;77:103–24.

Websites

www.acidbase.org
www.lakesidepress.com
www.merck.com
www.uchc.edu

Pituitary, Thyroid, and Adrenal Emergencies in the ICU

6

Harish Mallapura Maheshwarappa, P. Sabarish,
and Marutheesh Mallappa

Pituitary Apoplexy

Case Vignette

A 42-year-old diabetic man previously asymptomatic has been admitted to the emergency room (ER) with sudden-onset blurring of vision and vomiting with stable hemodynamics and Glasgow coma scale (GCS) E4V5M6. After stabilization and resuscitation in the ER, he underwent an MRI brain plain and contrast and was shifted to the ICU where he developed severe headache, hypotension, and drop in sensorium.

Pituitary apoplexy (PA) is defined as a clinical syndrome consisting of sudden onset of a severe headache, vomiting, and visual deterioration with or without altered mental status. It is usually caused by acute/subacute hemorrhage or infarction, most commonly of a pituitary tumor (adenoma or neuroendocrine tumor). The pathophysiology of PA and Sheehan's syndrome (postpartum pituitary apoplexy due to severe bleeding/hypotension) is summarized in Fig. 6.1.

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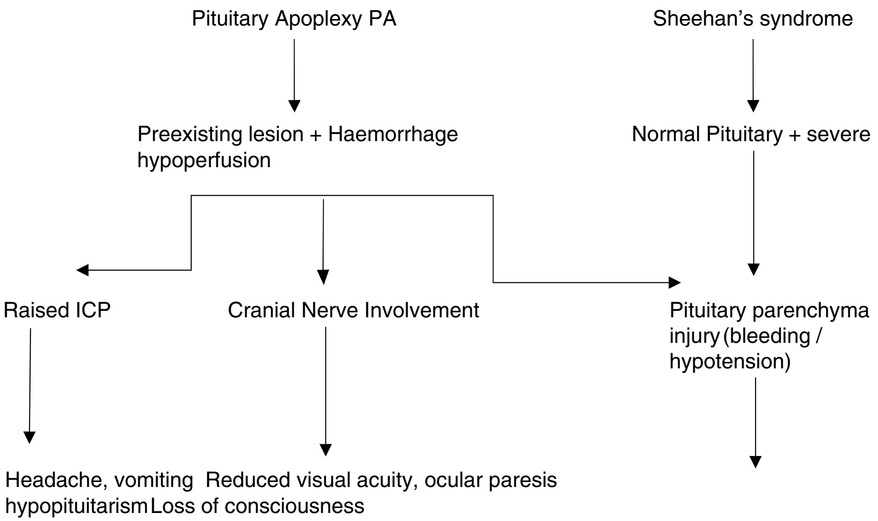
Pituitary Apoplexy PA
Sheehan's syndrome
Preexisting lesion + Haemorrhage hypoperfusion
Normal Pituitary + severe
Raised ICP
Cranial Nerve Involvement
Pituitary parenchyma injury (bleeding / hypotension)
Headache, vomiting
Reduced visual acuity, ocular paresis
hypopituitarism
Loss of consciousness

Fig. 6.1 Comparison between pathophysiologic mechanisms of pituitary apoplexy and Sheehan's syndrome

Step 1: Initial Assessment and Stabilization

A. Secure the airway and stabilize breathing for GCS less than 8.
B. Identify cause: Bleeding within the pituitary lesion, supply–demand mismatch in growing tumors leading to pituitary necrosis, rapid rise in blood supply (hypertensive crisis, raised intracranial pressure (ICP)), pituitary hormonal stimulation tests, rapid drop in blood supply (massive drop in blood pressure following massive hemorrhage, radiation, spinal anesthesia, etc.).

Step 2: Understand Probable Precipitating Factors

This includes diabetes, anticoagulants, hypertension, thrombocytopenia, coagulopathy, and pregnancy.

Step 3: Take History and Do a Physical Examination

- Clinical features depend on the speed of onset of infarction or hemorrhage and the volume of hemorrhage that directly influences the degree of compression of adjacent neuro-ophthalmologic structures and the pituitary gland.
- **Acute and severe (acute PA)** presents with sudden onset of severe retro-orbital, frontal, or suboccipital headache with nausea and vomiting and cranial nerve

symptoms such as diplopia, palpebral ptosis, and mydriasis with variable level of consciousness, serious neurological deficits, coma, and even death.

- **Subacute (subclinical PA)**, with milder symptoms developing over days or weeks with decreased visual acuity with visual field involvement ranging from small field defects to complete bilateral vision loss.
- The development of partial or complete hypopituitarism is common with similar hormone replacement needs for both groups [gonadotropin deficiency being the most common hormone deficiency (75%), followed by deficiency of corticotropin (70%) and thyrotropin (50%)]. Almost all patients with PA have growth hormone (GH) deficiency though not routinely tested.
- The sudden onset of adrenocorticotropic hormone (ACTH) and therefore cortisol deficiency is most serious as it can cause life-threatening hypotension.
- Low serum prolactin levels may correlate with a higher degree of pituitary dysfunction. Hyponatremia may be seen with central hypothyroidism, syndrome of inappropriate antidiuretic hormone secretion (SIADH), and adrenal insufficiency.

Step 4: Make a Diagnosis

- MRI is the preferred option (sensitivity of approximately 90%) because it can visualize and detect hemorrhage, necrosis, edema, and lesions within the pituitary gland, as also compression of the optic chiasm and other adjacent structures.
- CT scan if MRI unavailable/contraindicated.
- Visual acuity, visual field, and ocular motility should be assessed periodically at the patient's bedside during the first 48 h.
- Finally, electrolytes, renal function, liver function, coagulation, blood count, and pituitary function (cortisol, prolactin, free thyroxine, thyroid-stimulating hormone (TSH), IGF-1, GH, luteinizing hormone (LH), follicle-stimulating hormone (FSH), and estradiol in women of childbearing age or testosterone in men).

Step 5: Start Management

Conservative approach:

- It includes high-dose corticosteroids, hemodynamic stabilization, administration of hormone replacement therapy for hormonal deficiencies, medical management of functioning tumors (such as prolactinomas, acromegaly, and Cushing's disease), and specific treatment of any other underlying causes responsible for PA.
- Hydrocortisone 100–200 mg IV bolus followed by 2–4 mg every hour by continuous IV infusion or dexamethasone (2–16 mg per day) to reduce edema and treat central adrenal insufficiency.
- Antiedema measures and correction of coagulopathy in worsening Intracranial bleeds

Surgical approach:

- Urgently indicated in the decreased level of consciousness, hypothalamic involvement, sudden amaurosis, or loss of visual acuity. The transsphenoidal endoscopic approach is the preferred modality of choice preferably by experienced neurosurgeons. A craniotomy is indicated in larger suprasellar extension.
- Postprocedure monitor water and electrolyte imbalance along with improvement in visual symptoms and defects to be closely monitored.
- Pituitary apoplexy score (PAS) is utilized to justify the necessity for surgical decompression though it does not involve pituitary hormonal function.

Thyrotoxic Crisis/Thyroid Storm

A 61-year-old man was transferred from the ER to ICU after he was found to be in altered mental status associated with anxiety, agitation, fever, and chills of 1-day duration. The patient had a medical history of alcohol and polysubstance use disorder, iron deficiency anemia, and hyperthyroidism. He was sweating profusely, had palpitations, and was very restless. The patient had been diagnosed with hyperthyroidism about 3 years prior and had been on methimazole and propranolol. His heart rate was 160 bpm, the temperature was 39.8 °C, respiratory rate was 30 bpm, BP was 134/71 mmHg, and oxygen saturation was 95% on room air. The patient was uncooperative for a detailed neurological examination, but the rest of the physical examinations were normal.

Step 1: Identify the Syndrome and Underlying Etiology

- A thyroid storm, also known as a thyrotoxic crisis/thyrotoxicosis, is an acute, life-threatening complication of hyperthyroidism that presents with multisystem involvement with 8–25% mortality.
- The etiology of thyroid storm can be classified as follows:
  - **Thyrotoxicosis with a normal or high radioiodine uptake**: Autoimmune thyroid disease (AITD), Graves' disease (GD), hashitoxicosis, autonomous thyroid tissue, toxic adenoma (TA), toxic multinodular goiter (TMNG), TSH-producing pituitary adenoma, non-neoplastic TSH-mediated hyperthyroidism, human chorionic gonadotropin-mediated hyperemesis gravidarum, trophoblastic disease, and resistance to thyroid hormone (T3 receptor mutation).
  - **Thyrotoxicosis with a decreased or near-absent radioiodine uptake** Painless (silent, lymphocytic) thyroiditis, subacute (de Quervain's, granulomatous) thyroiditis, acute thyroiditis (due to amiodarone, radiation), and exogenous thyroid hormone intake.

Step 2: Understand the Pathophysiology of this Clinical Scenario

- Increased circulating levels of FT4 and an increase in target cell β-adrenergic receptor density or post-receptor modifications in signaling pathways leading to an increased sensitivity to catecholamines are possible hypotheses for thyroid storm.
- Triggering events for hyperthyroidism to convert to thyroid storm include surgical stress, infection, myocardial infarction, pulmonary embolism, drugs [amiodarone, iodine, antiviral (interferon-mediated injury], pregnancy, etc.

Step 3: Get Familiar with Clinical Symptomatology

- The transition of thyrotoxicosis to thyroid storm is relatively subjective and unclear. However, Burch and Warsofsky's scoring system was designed to assess degrees of dysfunction in various organ systems. However, due to its multisystem involvement and aggressive nature, it is prudent to treat it aggressively in the intensive care unit rather than focusing on definitions per se. Figure 6.2 shows the clinical spectrum of thyroid storm.

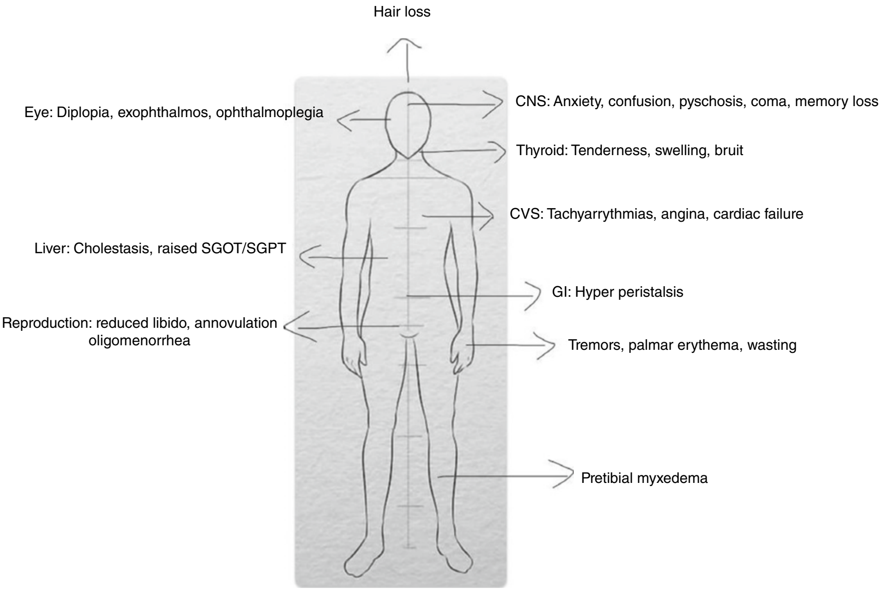
Hair loss
Eye: Diplopia, exophthalmos, ophthalmoplegia
CNS: Anxiety, confusion, pyschosis, coma, memory loss
Thyroid: Tenderness, swelling, bruit
CVS: Tachyarrythmias, angina, cardiac failure
Liver: Cholestasis, raised SGOT/SGPT
GI: Hyper peristalsis
Reproduction: reduced libido, annovulation oligomenorrhea
Tremors, palmar erythema, wasting
Pretibial myxedema

Fig. 6.2 Clinical spectrum of thyroid storm

Step 4: Send Investigations

Biochemistry

- Elevated FT3 and FT4 levels with reduced TSH levels.
- In 5% of patients, only T3 levels are high (T3 toxicosis).
- T3/T4 ratio >20 seen in Grave's disease and toxic multinodular goiter.
- T3/T4 ratio <15 seen in thyroiditis, iodine exposure, or exogenous levothyroxine intake.
- Elevated liver enzymes, hypercalcemia, and hyperglycemia, S cortisol (normal to lower ranges following ACTH stimulation test).

Imaging

- ECG: arrhythmias and tachycardia
- Echocardiography (cardiac failure)
- Noncontrast CT scan
- Doppler

Step 5: Start Management

Medical management of thyroid storm is summarized in Table 6.1.

Table 6.1 Medical management of thyroid storm

Inhibition of thyroid hormone synthesis (standard antithyroid drugs given at higher doses and more frequently)		
Methimazole	20–30 mg PO q6 h	Methimazole has a longer half-life so preferred for very critically ill.
Propylthiouracil (preferable)	200–400 mg PO q6–8 h	
		PTU decrease peripheral T4 → T3 conversion and safer during pregnancy (first trimester)
Inhibition of thyroid hormone release from the thyroid gland by iodine		
Saturated solution of potassium iodide (SSKI)	5 drops PO q6 h or 5–10 drops per rectum q6–8 h	A thionamide should be initiated before iodine therapy, to prevent the stimulation of new thyroid hormone synthesis
Lugol's solution	4–8 drops PO q6–8 h or 5–10 drops per rectum q6–8 h or 5–10 drops IV d q6–8 h	
Counteraction of peripheral effects of thyroid hormone		
Beta-blockers	**Prevents T4◇ T3 conversion peripherally**	
Propranolol	60–80 mg PO q4 h or 80–120 mg PO q6 h or 0.5–1 mg IV over 10–15 min; max 160 mg/day; adequate control of Heart rate target	
Atenolol	50–200 mg PO qday (or bd)	

(continued)

Table 6.1 (continued)

Metoprolol	100–200 mg PO qday (or bd)	
Nadolol	40–80 mg PO qday	
Esmolol	Loading dose of 250–500 µg/kg IV, then 50–100 µg/kg/ min IV	
Steroids	**Prevents T4◇ T3 conversion peripherally, vasomotor stability**	
Hydrocortisone	100 mg tid after 300 mg loading dose	
Dexamethasone	2 mg IV qid	
Supportive care		
Acitaminophen	325–650 mg PO	Avoid salicylates
Thiamine	200 mg IV BD	To prevent Wernicke's encephalopathy
IV fluids	5% D or 10% D	
Treating precipitating cause		

Treat precipitating factors

- *Alternative therapies:*
  - *Lithium:* 300 mg qid, prevents T4 release (maintain 0.6–1.0 mEq/L).
  - *Potassium perchlorate:* The perchlorate anion, ClO 4 −, is a competitive inhibitor of iodide transport (1 g daily) with MMI (30–50 mg daily) for up to 4 weeks have been used successfully without side effects such as aplastic anemia and nephrotic syndrome.
  - *Cholestyramine*: 4 g PO qid, prevents entero-hepatic circulation of thyroxine (if patient allergic to thionamide).
  - *Plasmapheresis*: removes thyroid binding globulin-bound T4 and antibodies against the thyroid gland. The effect is transient 24–48 h.
  - *Surgery:* patient intolerant of thionamide.

Myxedema Coma

Case Vignette

A 50-year-old female patient undergoing treatment for abdominal tuberculosis for the past three months presented with a history of mild abdominal distension, slightly altered sensorium, dry skin, and signs of jaundice. As imaging studies did not reveal any significant findings, a decision to proceed with diagnostic laparoscopy was taken. Meanwhile, her thyroid-stimulating hormone (TSH) report came as 75 mIU/ml, and as her sensorium deteriorated, she was transferred to the intensive care unit for further care.

Step 1: Suspect Myxedema Coma

- Myxedema coma, the severe form of hypothyroidism, is rare; however, when it occurs, it presents a potentially life-threatening condition (mortality rate 50–60%).
- It typically occurs in elderly, female patients who have not been previously treated, as well as those with inadequate or discontinued treatment (average age 75 years).
- The term myxedema coma is misleading, and decompensated hypothyroidism/myxedema crisis may be a more appropriate term for hypothyroidism leading to organ failure.
- The brain is the first organ to fail; hence, the main clinical feature is delirium.
- In myxedema coma, decreased mental status is caused by a combination of factors, including the direct impact of low thyroid hormone action in the central nervous system, cerebral anoxia and hypercapnia from respiratory insufficiency, hemodynamic instability leading to reduced brain perfusion, and electrolyte abnormalities.

Step 2: Identify Precipitating Factors and Disorders that Can Result in Hypothyroidism (Table 6.2)

Table 6.2 Precipitating factors and disorders that can result in hypothyroidism

Precipitating factors	Disorders that can result in hypothyroidism and myxedema coma
Hypothermia Infections, septicemia Myocardial infarction or congestive heart failure Stroke Surgery Respiratory depression due to drugs (e.g., anesthetics, sedatives, tranquilizers) Other medication: amiodarone, rifampin, phenytoin Withdrawal of levothyroxine Trauma, burns, or gastrointestinal blood loss	Chronic autoimmune (or Hashimoto's) thyroiditis Postsurgical hypothyroidism Postablative (^{131}I) hypothyroidism Neck irradiation Central hypothyroidism due to hypothalamic or pituitary disorder Drug-induced hypothyroidism Lithium, amiodarone, sunitinib Excessive consumption of goitrogenic foods, such as raw Chinese white cabbage (bokchoy)

Step 3: Understand Pathogenesis of Myxedema Coma (Fig. 6.3) Pathogenesis

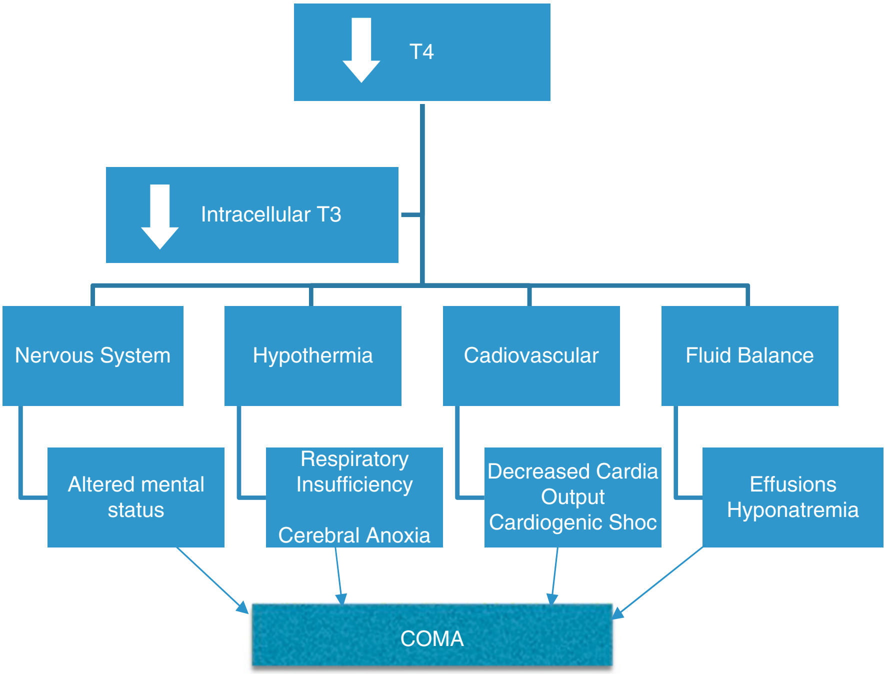
T4
Intracellular T3
Nervous System
Hypothermia
Cadiovascular
Fluid Balance
Altered mental status
Respiratory Insufficiency
Cerebral Anoxia
Decreased Cardia Output
Cardiogenic Shoc
Effusions
Hyponatremia
COMA

Fig. 6.3 Pathogenesis of myxedema coma

Step 4: Identify Clinical Presentation

- Neurological: altered mental state (poor cognitive function, psychosis, coma).
- Hypothermia (as low as 23 °C) or absence of fever with severe infection (prognosis worsens as the core temperature falls).
- Physical signs of hypothyroidism.
- Respiratory depression.
- Cardiac: hypertrophy, bradycardia, decreased ventricular contractility, hypotension, and ECG changes (low voltage, nonspecifc ST-wave changes and sometimes torsades de pointes with a long QT interval).
- GI: anorexia, abdominal pain, distention, and constipation.
- Biochemical abnormalities include hyponatremia, normal or increased urine sodium excretion, elevated CPK and LDH, hypercholesterolemia, hypoglycemia, normocytic or macrocytic anemia, deranged coagulation parameters. TSH values may only be modestly raised (and will be normal or low in secondary hypothyroidism) but free thyroxine levels are usually very low.

Step 5: Start Evaluation

Diagnosis

- Laboratory results will show elevated TSH and low free T4.
- TSH may not be as elevated as expected for the low level of free T4. This is usually due to intercurrent illness or the use of dopamine and/or glucocorticoids.
- On the other hand, a normal-to-low or low TSH coupled with a low free T4 value indicates central hypothyroidism, especially if associated with adrenal insufficiency and other clues such as inappropriately normal gonadotropins in postmenopausal women, or a history of pituitary surgery.
- Distinguishing between patients with myxedema coma caused by central hypothyroidism and those with nonthyroidal illness (“euthyroid sick”) syndrome, characterized by decreased mental status, can be challenging. The latter group may exhibit low TSH and low total T3 levels due to severe illness and medications administered during treatment.

Step 6: Manage Myxedema Coma?

Treatment

- Supportive measures include early mechanical ventilation when indicated, passive rewarming for hypothermia, vasopressor agents for hemodynamic instability, and standard intensive care.
- Appropriate fluid management and correction of hypotension and dyselectrolytemia.

- Aggressive management of precipitating factors and steroid supplementation: Stress doses of hydrocortisone (50 mg IV every 6–8 h) should be given due to the possibility of concomitant adrenal insufficiency, which occurs in 5–10% of cases. Giving thyroid hormone without steroid can precipitate adrenal crisis.
- Thyroid hormone replacement.

Rapid institution of thyroid hormone replacement:

- “High-dose” regimen options:
  - Intravenous thyroxine (T4) bolus of 300–500 mg, followed by 50–100 mg daily.
  - Oral thyroxine in higher doses (usually by nasogastric tube), as absorption may be impaired.
  - Tri-iodothyronine (T3) (10–20 mg initially, followed by 10 mg every 4 h for 24 h, then 10 mg every 6 h) instead of thyroxine, but has the potential to cause adverse cardiac effects when given too rapidly.
  - Give 200 mg thyroxine with 10 mg tri-iodothyronine initially, and then tri-iodothyronine 10 mg every 12 h and thyroxine 100 mg every 24 h, until the patient resumes normal thyroxine orally.
- “Low-dose” approach
- 25 mg of thyroxine daily for a week or 5 mg of tri-iodothyronine twice daily with a gradually increasing dose.

Adrenal Crisis

Case Vignette

A 20-year-old woman presented with a 3-month history of recurrent vomiting, occurring between 5 and 10 times daily, accompanied by significant weight loss. Upon admission, she exhibited signs of dehydration and was unable to maintain oral intake due to persistent nausea and vomiting. She described some right-sided abdominal pain and a pregnancy test was negative. The patient had a pre-existing diagnosis of hypothyroidism. Clinical examination revealed that she was markedly underweight, mild skin pigmentation tachycardia, and low blood pressure. Laboratory results indicated a sodium level of 133 mmol/L, random cortisol 2 nmol/L.

Step 1: Classify Adrenal Insufficiency (AI) and Identify the Causes for Primary Adrenal Insufficiency

- Primary adrenal insufficiency (Addison’s disease)
  - Presently autoimmune adrenalitis is the most common cause of Addison’s disease as incidence of TB is decreased. The other causes of primary adrenal insufficiency are given in Figs. 6.4 and 6.5

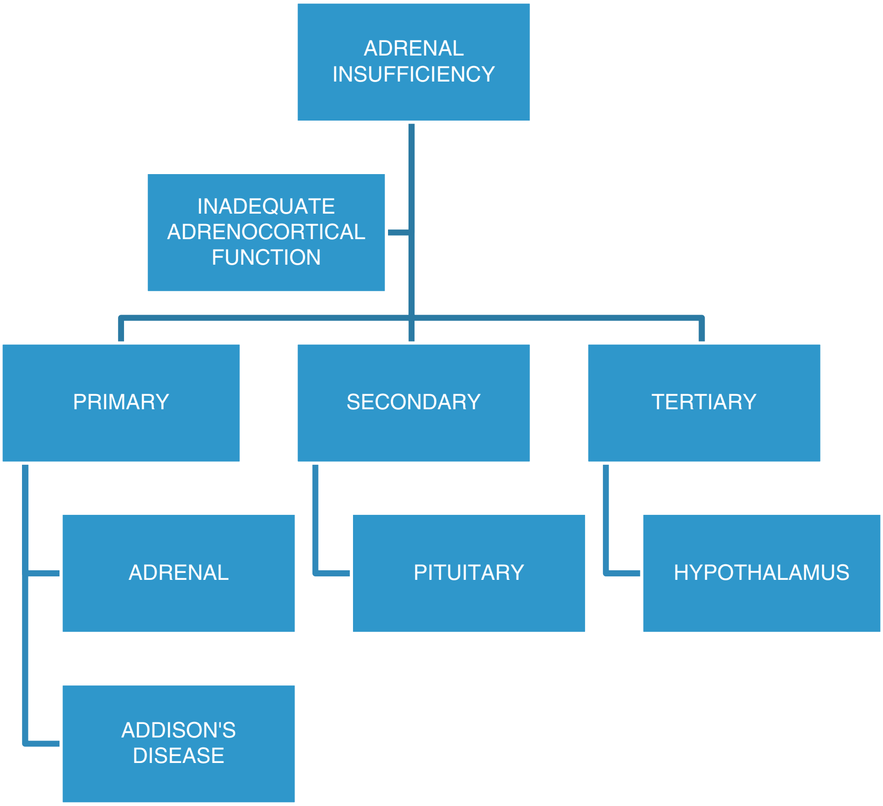
ADRENAL INSUFFICIENCY
INADEQUATE ADRENOCORTICAL FUNCTION
PRIMARY
SECONDARY
TERTIARY
ADRENAL
PITUITARY
HYPOTHALAMUS
ADDISON'S DISEASE

Fig. 6.4 Classification and causes of adrenal insufficiency

- Autoimmune—most common cause of AI, serum adrenal antibodies are common in fe\male, particularly those with polyglandular autoimmune syndrome (APS). Look for hypoparathyroidism, thyroid disease, and diabetes mellitus.
- Infections—tuberculosis, AIDS, fungal.
- Hemorrhage—septic shock—meningococcal waterhouse syndrome, APLA syndrome, and anticoagulants.
- Infiltrations—amyloidosis, sarcoidosis, hemochromatosis, and lymphoma.
- Metastasis.

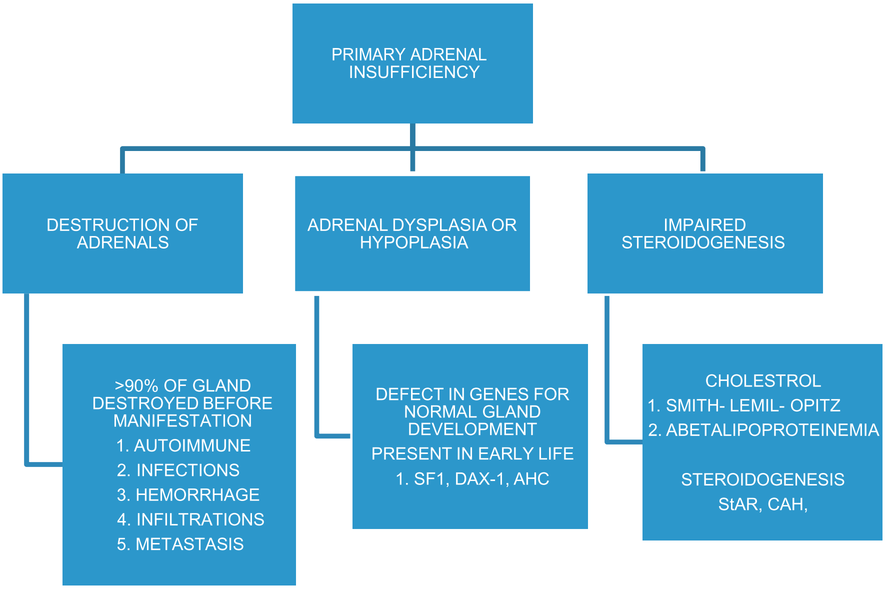
PRIMARY ADRENAL INSUFFICIENCY
DESTRUCTION OF ADRENALS
ADRENAL DYSPLASIA OR HYPOPLASIA
IMPAIRED STEROIDOGENESIS
>90% OF GLAND DESTROYED BEFORE MANIFESTATION
1. AUTOIMMUNE
2. INFECTIONS
3. HEMORRHAGE
4. INFILTRATIONS
5. METASTASIS
DEFECT IN GENES FOR NORMAL GLAND DEVELOPMENT
PRESENT IN EARLY LIFE
1. SF1, DAX-1, AHC
CHOLESTROL
1. SMITH- LEMIL- OPITZ
2. ABETALIPOPROTEINEMIA
STEROIDOGENESIS
StAR, CAH,

Fig. 6.5 Causes of primary adrenal insufficiency

Step 2: Identify Clinical Features of AI

Clinical features

- Adrenal crisis—fever, vomiting, abdominal pain, diarrhea, hypotension out of proportion to the severity of illness, confusion, and coma.
- Chronic insufficiency.
- General—generalized weakness, anorexia, weight loss, and salt craving.
- Cardiovascular system (CVS)—postural dizziness and hypotension.
- Gastrointestinal tract (GIT)—abdominal pain, vomiting, and diarrhea.
- Central nervous system (CNS)—headache, depression, and behavioral changes.
- SKIN—pigmentation.
- Sexual characteristics—loss of axillary and pubic hair, and loss of libido.

Step 3: Send Investigations

- High plasma renin, increased ACTH level, and low ACTH stimulated cortisol response.
- Biochemical—hyponatremia, hypoglycemia, hyperkalemia, azotemia, and hypothyroidism .
- Blood—eosinophilia and lymphocytosis.
- Cosyntropin stimulation test (Fig. 6.6)—Administer 250 mcg Cosyntropin—measure cortisol at 30 and 60 min, 2 samples at each point (total cortisol and free cortisol). Random serum cortisol measurement is not useful (secretion pulsatile).

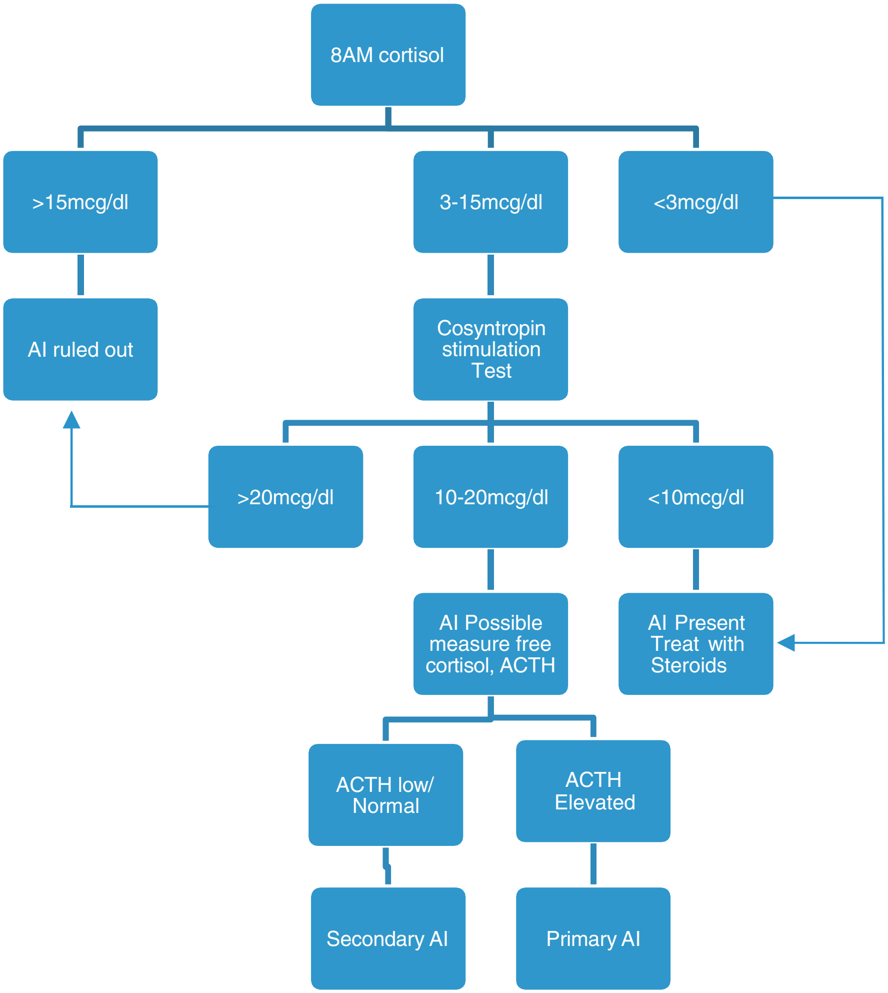
8AM cortisol
>15mcg/dl
3-15mcg/dl
<3mcg/dl
AI ruled out
Cosyntropin stimulation Test
>20mcg/dl
10-20mcg/dl
<10mcg/dl
AI Possible measure free cortisol, ACTH
AI Present Treat with Steroids
ACTH low/ Normal
ACTH Elevated
Secondary AI
Primary AI

Fig. 6.6 Cosyntropin stimulation test

Step 4: Initiate Management

Treatment

- Emergency measures: establish two large-gauge IV line.
- Send serum electrolytes, glucose, cortisol, and ACTH.
- Infuse initial resuscitative fluids 2–3 L, monitor for overload signs.
- Inj. hydrocortisone 100 mg stat followed by 50 mg sixth hourly or infusion of 200 mg/day after the initial bolus.
- 15 mg/h ideal. Step down gradually over 72 h and overlap with oral.
- Primary AI cases—begin mineralocorticoid replacement with fludrocortisone 0.1 mg daily.
- Search and treat the precipitating cause of crisis.
- Determine the type and cause of AI.
- Antibiotics if indicated.
- Taper glucocorticoids to maintenance doses over 1–3 days, if precipitating illness permits.

Step 5: Identify the Causes of Secondary AI?

Secondary AI
Cause for panhypopituitarism

- Sheehan's syndrome: Postpartum necrosis of pituitary gland failure to lactate and failure to menstruate. MRI brain—empty Sella sign.
- Post surgery—tumors.
- Radiation.
- Trauma.
- Developmental anomalies.

Pheochromocytoma Crisis

Case Vignette

A 35-year-old woman presented with a history of recurrent abdominal pain, anxiety, hypertension, dyslipidemia, obesity, and palpitations, for which she was under the care of a cardiologist. Additionally, the patient experienced tremors and reported weakness in her lower extremities. Her skin appeared pale on physical examination, but no other abnormalities were noted. Abdominal imaging revealed a suprarenal nodule measuring 31 mm in diameter.

Laboratory tests indicated elevated levels of urinary metanephrines at 1080 μg/24h (with a normal range below 341 μg/24h) and increased urinary normetanephrine at 734 μg/24h (normal range below 444 μg/24h).

Step 1: Identify Pheochromocytoma Crisis

- Pheochromocytoma crisis is a complex event that can be detected early and managed promptly to prevent a crisis. Sometimes, it is the first sign of the condition.
- Adrenal masses are being found more frequently due to the increased use of imaging methods, often through genetic testing.
- However, deciding on the best approach for testing and imaging can be challenging.
- World Health Organization (WHO) distinguishes between pheochromocytoma and paraganglioma primarily based on anatomical location as histological features alone do not differentiate these two tumor types sufficiently.

Step 2: Identify the Risk and Precipitating Factors (Table 6.3)

Table 6.3 Risk and precipitating factors for pheochromocytoma crisis

Risk factors in patients with underlying pheochromocytoma:	Precipitating factors
Spontaneous Associated conditions: Multiple endocrine neoplasia type 2 or neurofibromatosis type 1 Von Hippel–Lindau syndrome Ataxia telangiectasia Tuberose sclerosis Sturge–Weber syndrome	Spontaneous hemorrhage into pheochromocytoma Exercise Pressure on abdomen Urination of drugs: guanethidine, glucagon, naloxone, metoclopramide, ACTH, cytotoxics, and tricyclic antidepressants

Step 3: Understand Pathophysiology and Clinical Presentation

Pathophysiology

- The action of unopposed high circulating levels of catecholamines acting at adrenoreceptors:
  - Alpha-receptors cause a pressor response with increases in blood pressure.
  - Beta-receptor activation has positive inotropic and chronotropic effects.

Presentation

- The classic triad of symptoms—headaches, palpitations, and profuse sweating.
- Cardiovascular: hypertension, palpitations, and myocardial infarction.
- Autonomic: sweating, pallor, hyperhidrosis, nausea, and vomiting
- Psych/neuro: anxiety and tremulousness, a feeling of impending death, altered consciousness (hypertensive encephalopathy), pounding headache, and stroke.
- Abdominal: pain (tumor hemorrhage), paralytic ileus endocrine: hyperglycemia.

Step 4: Start Evaluation

Diagnosis

The diagnosis necessitates evidence of an overabundant discharge of catecholamines and anatomical verification of the tumor.

- Urine for estimation of 24-h free catecholamines and metanephrines.
- Plasma metanephrines and catecholamines.
- Metanephrine levels correlate well with tumor size. Failure to suppress plasma normetanephrine with clonidine is very supportive of the diagnosis of pheochromocytoma (97% sensitivity, 100% specificity).
- If metanephrines are elevated, perform contrast-enhanced.
- CT or MRI; if abdominal imaging is negative, consider an MRI of the skull base, neck, chest, and pelvis if the mass is >10 cm in diameter or is extra-adrenal, search for additional paragangliomas or metastatic disease with I-MIBG scintigraphy, Ga-DOTATATE–PET–CT, or 18F-FDG–PET–CT.
- To accurately detect catecholamine-secreting tumors, gradually reduce and stop tricyclic antidepressants and other psychoactive medications for at least 2 weeks before hormonal testing.

Step 5: Identify the Complications Associated with Pheochromocytoma

Complications

- Heart—angina heart attack, cardiomyopathies, and myocarditis
- Acute failure—Arrhythmias
- Brain—stroke and encephalopathy
- Kidney—acute kidney injury and hematuria
- Lungs—pulmonary edema, ARDS, pulmonary HTN

Step 6: Treat Pheochromocytoma Crisis?

Treatment

- Surgical resection is typically the preferred treatment, but the preparation and scheduling of the procedure are often ambiguous.
- It is recommended that all patients undergo genetic analysis. Once the mutation is detected, the specific gene will dictate the customization of imaging studies and subsequent medical care.
- Do not wait for biochemical confirmation—start treatment.
- Treatment of the hypertensive crisis should be carried out in an intensive care unit when possible.
- Nitroprusside is the first line of therapy with an initial intravenous dose of 0.3 μg/kg/min. Increase by 0.1–0.3 μg/kg/min at 3–5 min intervals until the hypertension is controlled. The maximum recommended dose is 10 μg/kg/min.
- Phentolamine, a nonselective α-adrenoceptor antagonist. The usual dose for adults is 5 mg intravenously, which can be repeated every several minutes until the blood pressure is controlled.
- Patients with tachyarrhythmia should receive a β-adrenoceptor antagonist. IV labetalol at an initial dose of 20 mg over 2 minutes. Additional doses of 40 mg, up to 80 mg, can be administered at 10-minute intervals until the tachycardia is controlled. The total dose should not exceed 300 mg in a 24 h period.
- Alternatively, IV metoprolol 2.5–5.0 mg every 6–12 h and titrated as needed up to 15 mg every 3 h.
- Once satisfactory control of the hypertensive crisis is achieved, treatment is transitioned to oral phenoxybenzamine, an α-adrenoceptor antagonist, 10 mg twice daily, adjusted upward in 10 mg increments every 2 or 3 days, to a maximum of 50–100 mg 3 times daily. Intravenous β-adrenoceptor blockade can be transitioned to oral atenolol 25–50 mg every 8–12 h.

Suggested Reading

Bahn R, Burch H, Cooper D, et al. Hyperthyroidism and other causes of thyrotoxicosis: management guidelines of the American thyroid association and American Association of clinical endocrinologist. Thyroid. 2011;21(6):593–646.

Dabon-Almirante CL, Surks M. Clinical and laboratory diagnosis of thyrotoxicosis. Endocrinol Metab Clin North Am. 1998;27(1):25–35.

Donangelo I, Braunstein GD. Myxedema coma. In: Endocrine emergencies: recognition and treatment; 2021. p. 93–10.

Dubuisson AS, Beckers A, Stevenaert A. Classical pituitary tumour apoplexy: clinical features, management and outcomes in a series of 24 patients. Clin Neurol Neurosurg. 2007;109(1):63–70.

Goldfarb-Rumyantzev A. Endocrinology issues in critical care. In: Critical care medicine: an algorithmic approach; 2021. p. 242.

Karger S. Thyroid storm—thyrotoxic crisis: an update. Dtsch Med Wochenschr. 2008;133(10):479–84.

Nayak B, Burman K. Thyrotoxicosis and thyroid storm. Endocrinol Metab Clin North Am. 2006;35:663–86.

Neumann HP, Young WF Jr, Eng C. Pheochromocytoma and paraganglioma. N Engl J Med. 2019;381(6):552–65.

Rajasekaran S, Vanderpump M, Baldeweg S, et al. UK guidelines for the management of pituitary apoplexy. Clin Endocrinol (Oxf). 2011;74(1):9–20.

Rushworth RL, Torpy DJ, Falhammar H. Adrenal crises: perspectives and research directions. Endocrine. 2017;55:336–45.

Rushworth RL, Torpy DJ, Falhammar H. Adrenal crisis. N Engl J Med. 2019;381(9):852–61.

Tischler AS, de Krijger RR, Gill AJ, et al. Phaechromocytoma. In: WHO classification of tumours of endocrine organs. 4th ed. Lyon, France: International Agency for Research on Cancer; 2017. p. 18390.

Verrees M, Arafah BM, Selman WR. Pituitary tumor apoplexy: characteristics, treatment, and outcomes. Neurosurg Focus. 2004;16(4):E6.

Glycemic Control in the ICU

7

Rajesh Chawla, Subhash Todi, and Prashant Nasa

Case Vignette

A 45-year-old male patient was admitted to hospital with cough, breathlessness, dizziness, and fever for the past 5 days. He was hypoxemic (SpO_2 88% on a nonrebreathing mask) and hypotensive (blood pressure 82/34 mmHg after 2 L of IV fluid). He was intubated and started on mechanical ventilation. His blood glucose was 350 mg/dL on the glucometer.

Hyperglycemia is commonly seen in both diabetic and nondiabetic patients in ICUs. Hyperglycemia is also an independent risk factor for mortality and morbidity in medical and surgical ICU patients. Various factors contribute to hyperglycemia in the ICU. These include increased counterregulatory hormones (glucagon and cortisol), hepatic insulin resistance, glucocorticoid therapy, dextrose-containing solutions, and high-calorie enteral and parenteral nutrition. It is also believed to be a marker of more severe disease.

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Step 1: Check Blood Glucose

- Check capillary glucose by point-of-care properly calibrated glucometer.
- Caution is required in interpreting results of point-of-care glucometer in patients with anemia, polycythemia, hypoperfusion, or use of medications that can interfere with glucose measurements.
- Arterial glucose (in patients with arterial line) or venous glucose measured in a laboratory glucose analyzer may be more accurate in patients with shock on vasopressors or hypoxia or anemia.
- Treatment for hypoglycemia/hyperglycemia should not be withheld while one is waiting for a laboratory glucose value.

Step 2: Assess Glycemic Risk

- Patients should be asked about their history of diabetes, current treatment for diabetes recent blood sugar, and HbA1c levels.
- Check for HbA1c to assess control of glycemia.
- Check comorbidities such as hypertension, renal disease, liver disease, pancreatitis, chronic obstructive airway disease (COAD), obesity, and coronary artery disease.
- Enquire about medication history causing hyperglycemia—corticosteroids, octreotide, β-blockers, thiazide diuretics, niacin, protease inhibitors, and antipsychotic agents.
- If diabetic enquire about oral hypogylcemics or insulin regimen.

Step 3: Decide on the Frequency of Blood Glucose Measurement

- All hemodynamically unstable patients, especially those on intravenous insulin infusion, should have blood glucose checked every hour or even more frequently.
- As the condition stabilizes or in less sick patients, this interval may be prolonged.
- With any change in the patient's condition or nutrition delivery regimen, initiate more frequent glucose monitoring.

Step 4: Decide on the Target Blood Glucose Level

- The present recommendation in general medical/surgical ICU patients is to keep blood glucose between 140 and 180 mg/dL. Current SCCM recommendation is to keep target 140 mg to 200 mg/dL.
- Patients with an expected length of stay for more than 3 days in ICU will benefit from this control.

- For patients with shorter stays, it may have a more liberal target sugar control.
- A more liberal blood sugar control is also advised in patients who are diabetic because of the risk of relative hypoglycemia.

Step 5: Decide on an Insulin Delivery Route

- All oral hypoglycemic agents should be discontinued during the initial days of instability.
- Intravenous infusion of short-acting regular insulin is the treatment of choice in critically ill patients.
- Basal insulin (long-acting insulin) could be restarted as soon as the patient is stabilized and started on enteral nutrition for better glycemic control.
- The following groups of patients may be candidates for periodic subcutaneous insulin:
  - Step-down therapy from intravenous insulin
  - Less sick patients on oral diet

Step 6: Decide on Insulin Delivery Protocol (Tables 7.1 and 7.2)

- Insulin protocol should be institution-specific and nurse-driven.
- All efforts should be made to educate nurses and residents and ensure compliance by periodic audits.
- Dynamic insulin protocols, ideally computerized, which can monitor trend of rise or fall of blood glucose and adjust insulin doses, tend to keep blood glucose at a more desirable range.

Table 7.1 An example of an algorithm of IV insulin therapy in a critically ill patient

	Initiation		Maintenance	
Random blood sugar (RBS) (mg/dL)	Bolus (U)	Infusion (U/h)	At 1–5 U/h	At >5 U/h
151–199	0	2	Increase 1 U/h	Incr 2 U/h
200–249	3	2	Bolus 3 U + incr 1 U/h	Bolus 3 U + incr 2 U/h
250–299	5	3	Bolus 5 U + incr 1 U/h	Bolus 5 U + incr 2 U/h
300–349	8	3	Bolus 8 U + incr 1 U/h	Bolus 8 U + incr 2 U/h
350–399	10	4	Bolus 10 U + incr 2 U/h	Bolus 10 U + incr 3 U/h
400–449	10	5	Bolus 10 U + incr 3 U/h	Bolus 10 U + incr 4 U/h
>450	10	6	Bolus 10 U + incr 4 U/h	Bolus10 U + incr 4 U/h

Target random blood sugar: 140–180 mg/dL

Table 7.2 Another example of algorithm of IV insulin therapy in a critically ill patient

RBS (mg/dL)	Scale 1 (IV—U/h)	Scale 2 (IV—U/h)	Scale 3 (IV—U/h)	Scale 4 (IV—U/h)
<64	Treat as hypoglycemia	Do	Do	Do
64–140	Nil	Nil	Nil	Nil
141–200	1	2	3	4
201–250	2	4	6	8
251–300	3	6	9	12
301–350	4	8	12	16
351–400	5	10	15	20
>400	10	15	20	25

The patient should be started on a particular scale depending on initial sugar and clinical scenario. In this scale, in order to arrive at a target glucose level of 140–180 mg/dL, insulin infusion rate should be shifted horizontally to the next or previous scale in the same row if sugar remains within the range for that row. If sugar increases or decreases to the other range, the infusion rate should be shifted vertically for that range in the same scale

Target random blood sugar: 140–180 mg/dL

- Use insulin delivery protocol as per Table 7.1. For example, A diabetic patient with admission blood sugar of 250 mg/dL should get 5 U regular insulin bolus followed by 3 U/h. of insulin infusion. Next blood sugar after 1 h is 270 mg/dL, another bolus of 5 U regular insulin and increase insulin infusion to 4 U/h.
- Another insulin delivery protocol that can be used is described in Table 7.2, for example, a diabetic patient with admission blood sugar of 250 mg/dL and normal renal function may be started on scale 2 at 4 U/h. Patients with impaired renal function could be started on scale 1 and nondiabetic patients on scale 3 or 4. Next blood sugar check after 1 h is 270 mg/dL, the scale should shift vertically down (range 251–300) and infusion increased to 6 U/h. Next blood sugar is 264 (target 140–180 mg/dL); the scale should shift horizontally to the right to the infusion rate of 9 U/h.
- Intermittent sliding scale subcutaneous insulin in less sick patients with mild hyperglycemia.

Step 7: Avoid Hypoglycemia (Blood Glucose <70 mg/dL)

- Rigorous blood glucose control (80–110 mg/dL) leads to hypoglycemic episodes in a mixed medical/surgical ICU, which may be detrimental to their outcomes.
- The following groups of patients are more prone to hypoglycemia:
- Renal failure
- Dialysis
- Liver failure
- Malnourished
- Adrenal insufficiency
- Intolerance to enteral feed

- Stop insulin infusion immediately and give 50 mL of 25% dextrose intravenously and repeat this till blood glucose is more than 90 mg/dL and the patient is asymptomatic.
- Check blood glucose every 15 min and then decrease the frequency depending on clinical response.
- Ensure adequacy of carbohydrate calorie intake either enterally or parenterally and avoid abrupt discontinuation.

Step 8: Avoid Large Variations in Glucose Concentrations in the ICUs

- Glycemic variability is expressed as the standard deviation of each patient's blood glucose levels.
- Glycemic variability is an independent predictor of mortality in a heterogeneous population of ICU patients.
- The efficacy of continuous or near-continuous glucose monitoring and/or new algorithms targeted more specifically to reduce glycemic variability as well as mean blood glucose requires further clinical studies in ICU patients before the final recommendation is made.

Step 9: Avoid Under- or Overtreatment and Safety Issues

- Overtreatment and undertreatment of hyperglycemia represent major safety concerns.
- Education of ICU staff is essential in engaging the support of those involved in the care of inpatients with hyperglycemia.
- Regular audit and process measures should be undertaken to assess compliance with insulin regimens and attainment of target glucose range, avoidance of hypoglycemia, and minimizing glycemic variability.

Step 10: Change to Intermittent Treatment Once Stable

- Switch over to subcutaneous insulin.
- Long-acting insulin should overlap with discontinuation of insulin infusion to prevent hyperglycemia.
- Intermittent short-acting insulin (either a fixed dose or based on sliding scale) pre meals or six hourly should be instituted.
- Calculate the dosage taking into account the history of diabetes, type of diabetes, previous insulin dose, stress level, steroid use, risk of hypoglycemia, and general clinical status.

Suggested Reading

Arnold P, Paxton RA. The effect of a hypoglycemia treatment protocol on glycemic variability in critically ill patients. J Intensive Care Med. 2015;30(3):156–64. *Treatment of hypoglycemia with dextrose 50% can overcorrect blood glucose levels and increase glucose variability. This study evaluated the effect of a hypoglycemia treatment protocol focused on minimizing glucose variability in critically ill patients. Implementation of a hypoglycemia treatment protocol led to a reduction in glucose variability, while still providing a safe and effective way to manage hypoglycemia in critically ill patients*

Evans L, Rhodes A, Alhazzani W, et al. Surviving sepsis campaign: international guidelines for management of sepsis and septic shock 2021. Intensive Care Med. 2021;47(11):1181–247. *Guidelines on glycemic control in sepis patients*

Honarmand K, Sirimaturos M, Hirshberg EL, et al. Society of Critical Care Medicine Guidelines on Glycemic Control for Critically Ill Children and Adults 2024. Crit Care Med. 2024;52(4):e161–81. *Current SCCM guidelines*

Juneja D, Deepak D, Nasa P. What, why and how to monitor blood glucose in critically ill patients. World J Diabetes. 2023;14(5):528–38. *The review highlights the challenges associated with blood glucose monitoring in critically ill patients, various indices related to glycemic control, targets of blood glucose and recent advances in blood glucose monitoring*

Kalfon P, Giraudeau B, Ichai C. Tight computerized versus conventional glucose control in the ICU: a randomized controlled trial. Intensive Care Med. 2014;40(2):171–81. *A multi-center randomized trial in 34 French ICU. Adult patients expected to require treatment in the ICU for at least 3 days were randomly assigned without blinding to undergo tight computerized glucose control with the or conventional glucose control with blood glucose targets of 4.4-6.1 and <10.0 mmol/L, respectively. The primary outcome was all-cause death within 90 days after ICU admission. Primary outcome was available for 1,335 and 1,311 patients, respectively.The conclusion was that tight computerized glucose control with the computerised algorithm did not significantly change 90-day mortality and was associated with more frequent severe hypoglycemia episodes in comparison with conventional glucose control*

Kavanagh BP, McCowen KC. Glycemic control in the ICU. N Engl J Med. 2010;363(6):2540. *A clinical problem-solving article with literature review*

NICE-SUGAR Study Investigators for the Australian and New Zealand Intensive Care Society Clinical Trials Group and the Canadian Critical Care Trials Group. Intensive Care Med. 2015;41(6):1037–47. *Randomized trial of target blood glucose (BG) range of either 4.5-6.0 mmol/L (intensive control) or <10 mmol/L (conventional control). Subgroup analysis of traumatic brain injury (TBI) and extended Glasgow outcome score (includes mortality) at 24 months. Patients with traumatic brain injury randomly assigned to intensive compared to conventional glucose control experienced moderate and severe hypoglycemia more frequently, no significant difference in other clinically important outcomes was noticed.*

von Loeffelholz C, Birkenfeld AL. Tight versus liberal blood-glucose control in the intensive care unit: special considerations for patients with diabetes. Lancet Diabetes Endocrinol. 2024;12(4):277–84. https://doi.org/10.1016/S2213-8587(24)00058-5. *A recent review article discussing the challenges of glycemic control in ICU patients. In most patients, insulin should be initiated with persistent blood glucose concentrations higher than >180 mg/dL, targeting a range of 140-180 mg/dL. Liberal blood glucose targets of 252 mg/dL may be considered, particularly in critically ill patients with poor prehospital glycaemic control, substantial comorbidities, previous hypoglycaemia, and frailty. Howver, recent data from observational studies suggest an increased mortality with liberal glucose control among patients with admission* HbA_{1c} *of less than 6·5% and more stringent targets of 110-140 mg/dl may be considered in such patients, as long as this is achieved without hypoglycemia*

Diabetic Emergencies

8

Sandhya Talekar and Urvi Shukla

Case Vignette

An 18-year-old female patient presents with high-grade fever, tachypnea, and altered mentation to the emergency department. She had diarrhea for 3 days that was watery and large in volume. On examination, she was found to be febrile with a temperature of 101 °F. Her pulse rate was 130/min regular, and her blood pressure was 90/70 mmHg. She had a Glasgow coma score of 9. Her random plasma glucose on arrival was 480 mg/100 mL. She was not known to have diabetes.

Diabetic ketoacidosis (DKA) and hyperosmolar hyperglycemic state (HHS) are serious metabolic complications of diabetes and can occur in both type I and II diabetic patients. Insulin deficiency, increased insulin counter-regulatory hormones (cortisol, glucagon, growth hormone, and catecholamines), and peripheral insulin resistance lead to hyperglycemia, dehydration, ketosis, and electrolyte imbalance, which underlie the pathophysiology of DKA. DKA usually occurs in young patients with type 1 diabetes who are insulin-dependent, and HHS usually occurs in the elderly with type 2 diabetes on either oral hypoglycemic agents or insulin. The basic pathophysiological difference is the absence of circulating insulin in DKA and the presence of some residual insulin function in HHS, which prevents lipolysis, and ketosis. Recently, the use of sodium-glucose co-transporter 2(SGLT-2) inhibitors is known to increase the risk of DKA in type 1 and also type 2 diabetes known as

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euglycemic DKA as blood glucose levels are relatively normal in these patients due to glycosuria. The most common precipitating causes of DKA are infections, missed Insulin doses, and new-onset diabetes.

On average, patients with DKA/HHS may have the following deficit of water and key electrolytes per kg of body weight: free water 100 mL/kg; sodium 7–10 mEq/kg; potassium 3–5 mEq/kg; chloride 3–5 mmol/kg; and phosphorus 1 mmol/kg.

Hyperglycemic Emergencies

DKA and HHS

Diagnostic criteria for DKA (Table 8.1) and HHS (Table 8.2) have been modified to include the category of patients who have euglycemic DKA. The incidence is up to 10% and includes the use of SGLT-2 inhibitors as a risk factor. Even though hyperglycemia is still a diagnostic criterion, the range of blood sugar can vary widely and the new definition tries to incorporate the same.

Diagnostic criteria for HHS include hyperglycemia, hyperosmolarity with the absence of severe ketonemia, and acidosis. All four criteria must be present. Almost 30% of patients will have a combination of DKA/HHS criteria fulfilled.

Table 8.1 DKA diagnostic criteria

Hyperglycemia	Blood glucose > 200 mg/dL or previous history of diabetes
Ketosis	Urine ketone > 2+ OR serum B-hydroxybutyrate > 3.0 mmol/L
Acidosis	pH < 7.3 and/or Bicarbonate < 18 mmol/L

Table 8.2 HHS diagnostic criteria

Hyperglycemia	Blood glucose > 600 mg/dL
Hyperosmolarity	Calculated effective serum osmolarity > 300 mosmol/kg (2xNa mmol/L + glucose in mmol/L) OR Total serum osmolarity > 320mOsmol/kg (2xNa in mmol/L + Glucose in mmol/L + Urea in mmol/L)
Ketones	Urine ketone < 2+ OR serum B-hydroxybutyrate < 3.0 mmol/L
Acidosis	pH > 7.30 and bicarbonate > 15

Step 1: Start Initial Resuscitation (Refer Chap. 24)

- Urgently insert two wide-bore intravenous peripheral catheters for volume infusion.
- Draw blood samples for metabolic and other relevant tests.
- A central line may be needed in the presence of hypotension, lack of peripheral access, multiple infusions, severe acidosis, and impaired cardiorespiratory or renal parameters.
- For patients having signs of shock, administer IV isotonic fluid (0.9% saline or buffered crystalloid like Ringer's Lactate) as quickly as possible.
- In patients with mild hypovolemia, give fluid replacement as per individual needs.
- Ensure that the patient has no previous renal or cardiac morbidity.
- Serum potassium should be >3 mEq/L before insulin therapy is started.

Step 2: Take a Focused History and Perform a Physical Examination

- History of omitted insulin doses, alcohol binge, use of recreational drugs, especially cocaine, known history of diabetes, previous hospitalizations—all may point toward a diagnosis.
- The earliest symptoms of significant hyperglycemia are polyuria, polydipsia, and weight loss. Common early indicators of ketoacidosis are nausea, vomiting, abdominal pain, and hyperventilation.
- As hyperglycemia worsens, neurological symptoms may develop, potentially advancing to lethargy, focal deficits, obtundation, seizures, and coma.
- Frequent causes of diabetic ketoacidosis (DKA) include infection, nonadherence to insulin therapy, improper adjustment or discontinuation of insulin, new-onset diabetes mellitus, and myocardial ischemia.
- Table 8.3 points to general differences between the two syndromes.
- Hyperglycemia could also be the first presentation for young individuals without a history of diabetes.
- A thorough physical examination may help in finding a cause/possible focus of infection, which is often a trigger for the hyperglycemic crisis.

Table 8.3 Differences between DKA and HHS

DKA	HHS
Develops over hours to days	Develops over weeks
Usually alert	More likely to be obtunded
Nausea, vomiting and abdominal pain	Co-existing other illness
Kussmaul respiration	

Step 3: Send Essential Investigations

- Complete blood count with differential count.
- Arterial blood gas with anion gap.
- Urinalysis and urine ketones by dipstick.
- Metabolic panel to include electrolytes along with Mg and phosphates.
- Blood urea nitrogen and plasma creatinine (may be spuriously high due to chemical analysis interference with ketones).
- Serum ketones—B-hydroxybutyric acid levels.
- Electrocardiogram, chest X-ray.
- Screening for a possible infectious source.

Step 4: Fluid Therapy

- Management of DKA and HHS includes replacing lost fluid volumes, administration of insulin, electrolyte replacement, and treatment of the underlying cause.
- Patients with DKA and HHS usually have severe hypovolemia due to hyperglycemia, leading to osmotic diuresis.
- Average fluid loss in DKA and HHS is 8–10 L. HHS may result in fluid losses exceeding 10 L sometimes. The goal is to replace the total volume loss within 24–36 h with 50% of resuscitation fluid being administered during the first 8–12 h.
- In hypotensive patients, use crystalloids with vasopressors to restore circulating volume.
- For hypovolemia with shock, fluids should be infused as quickly as possible to reverse shock.
- Crystalloids are the initial fluids of choice irrespective of sodium levels. For hypovolemia without shock, fluid resuscitation is initiated with 15–20 mL/kg/h of 0.9% NS or balanced crystalloid in the first hour and then 500–1000 mL per hour for the next 2–4 h.
- After replacing the circulatory volume, fluid replacement rates can be reduced to 4–14 mL/kg/h. The type of fluid will be decided by hemodynamic stability, sodium levels, and fluid input–output balance.
- Once intravascular volume is restored and corrected, serum sodium is normal or elevated, administer half-normal saline (0.45%) at 250–500 mL per hour.
- In patients with low corrected serum sodium, continue with isotonic saline until hyponatremia resolves.
- in DKA, blood sugar level should drop to <250 mg/dL in 4–8 h. Once it is less than 250 mg/dL, replacement fluid should contain 5–10% dextrose in addition to isotonic fluids to prevent hypoglycemia and allow insulin infusion till ketonemia resolves.
- In patients with HHS, comorbidities like renal and cardiac dysfunctions warrant more close monitoring of hemodynamics.

- The usual time to correct hyperglycemia is 8–10 h, and reduction in glucose should not exceed 90–120 mg/dL/h to avoid cerebral edema.
- The rate of sodium decline should not exceed 10 mmol/L in 24 h, and the rate of fall of osmolality no greater than 3.0–8.0 mOsmol/kg/h.
- Rapid correction of sodium and osmolality may risk cerebral edema more so in pediatric patients.
- Volume resuscitation will enable renal losses of glucose and enhance peripheral action of insulin.
- Replace total body water losses slowly with 5% glucose solution (50–200 mL/h) once circulating volume and serum sodium are restored (usually when the blood glucose falls to <200 mg/dL). This is to avoid sudden osmolality changes, which may lead to cerebral edema and convulsions, seen more frequently in the pediatric age group.

Step 5: Correct Electrolyte Abnormalities

- Hyperglycemia may cause dilutional hyponatremia, so measured serum sodium is corrected by adding 2 mEq/L (2 mmol/L) for each 100 mg/dL (5.6 mmol/L) elevation of serum glucose over 100 mg/dL (5.6 mmol/L).
- The average sodium loss is 400–700 mmol, and the average potassium loss is 250–400 mmol in DKA.
- Replacement of serum potassium should begin early in the management of DKA as serum potassium concentration does not accurately reflect total body potassium.
- Potassium replacement should begin as soon as serum potassium concentration is less than 5.0 mEq/L. The target potassium concentration is 4–5 mEq/L.
- Ensure adequate urine output before replacing intravenous potassium.
- Guideline for replacing potassium is as follows:
  - If serum potassium is less than 3.5 mEq/L, give potassium at 20 mmol/h and insulin therapy should be delayed until potassium levels increase>3.5 mmol/L (given diluted in a liter). Patients with severe hypokalemia may need more intensive potassium replacement (e.g., 30 mEq per hour, possibly via central venous access) to raise serum potassium levels above 3.5 mEq/L.
  - If K is 3.5–5.0 mEq/L, give K at 10–20 mmol/h.
  - If K is more than 5.0 or anuric, no supplements are required.
- Potassium should be added to 0.45% saline instead of 0.9% saline to avoid hypertonicity of infused fluid. Correction of hyperosmolarity, acidosis, volume expansion, and insulin treatment leads to intracellular shifts in potassium and hypokalemia. Very low serum potassium levels should be avoided at all costs as they can lead to arrhythmias and have prognostic implications.
- Hypomagnesemia occurs early in the course of DKA and requires correction. Monitor serum magnesium levels.

- Phosphorous depletion is common in DKA due to urinary losses. Replacement is advised when it is severely depressed (<1 mg/dL). In patients with serum phosphate less than <1 mg/dL, add 20–30 mEq potassium phosphate to IV fluids. Routine replacement of phosphate is not known to show any beneficial effects on clinical outcomes and is associated with hypocalcemia and hypomagnesemia.
- Sodium bicarbonate infusion: Metabolic acidosis improves with restoration of intravascular volume and tissue perfusion. There is a limited role of bicarbonate therapy as it has not been shown to improve outcomes in DKA. Moreover, bicarbonate therapy is associated with adverse effects such as increased paradoxical intracellular and cerebrospinal fluid acidosis, increased CO_2 production, adverse effects on tissue oxygenation, risk of hypokalemia, and post-resuscitation metabolic alkalosis.
- Bicarbonate therapy may be considered in the following situations:
  - When pH is persistently less than 7.0 after 2–3 h of treatment.
  - When the hypotensive shock is unresponsive to rapid fluid replacement and persistent severe metabolic acidosis. If indicated, 100 mL of sodium bicarbonate 8.4% solution in 400 mL of sterile water (isotonic fluid) may be infused to achieve a pH > 7.0.
- Even in these circumstances, bicarbonate can only “buy time” until other treatments correct acidosis.

Step 6: Start Intravenous Insulin Infusion

- Insulin therapy should be started only after fluid and electrolyte resuscitation is underway and serum potassium is >3.5 meq/l to avoid precipitous fall of serum potassium. Short-acting insulin given by continuous infusion is the preferred choice.
- Use regular (rapid-acting) insulin as 0.1 U/Kg body weight as a bolus dose and then 0.1 U/kg/h as a continuous infusion or 0.14 U/Kg body weight as a continuous infusion without a bolus dose.
- When plasma glucose reaches 200–250 mg/dL, the insulin rate can be decreased by 50% or to the rate of 0.02–0.05 U/kg/h. If the blood glucose level does not decrease by 50–75 mg/dL/h, the rate of insulin infusion should be doubled.
- Rate of reduction of blood glucose should be less than 50–75 mg/dL/h.
- Maintain serum glucose between 150 and 200 mg/dL until resolution of DKA.
- Rapid correction of blood glucose levels could lead to cerebral edema seen mainly in the pediatric population, which can lead to convulsion and electrolyte disturbances (hypokalemia, hypomagnesemia, and hypophosphatemia).
- For patients presenting with normoglycemic DKA, the initial treatment is similar to that for mild-to-moderate DKA, with the following adjustments:
  - Start dextrose (5–10%) immediately with IV fluids and initiate it alongside insulin therapy.
  - Avoid giving a rapid-acting insulin bolus.
  - Begin insulin at a dose of 0.05 units/kg per hour or 0.1 units/kg every 2 h.

Step 7: Monitor the Effectiveness of Therapy Clinically and Biochemically

- The following features indicate clinical improvement:
  - Increased sense of well-being, reduced tachycardia and tachypnea
  - Improved mental status and able to eat orally
- The following biochemical parameters suggest resolution of DKA:
  - Serum glucose below 200 mg/dL in DKA
  - Serum bicarbonate more than 18 mEq/L
  - Venous pH more than 7.30
  - Serum anion gap less than 12 mEq/L (may not be accurate in patients receiving large volumes of 0.9% NS)
  - Delta anion gap/delta bicarbonate: As anion gap acidosis is replaced by nonanion gap hyperchloremic acidosis due to normal saline resuscitation and a paradoxical fall in pH, this ratio becomes >1 and is not a feature of worsening DKA.
  - Decreasing urine sugar.
  - Urine or serum ketones by nitroprusside test are not reliable parameters to follow as this test predominantly measures acetoacetate and acetone, whereas β-hydroxybutyrate is the predominant ketone in severe DKA, which is not measured usually in the laboratory. There may be a paradoxical rise of serum or urinary ketones as patients improve due to the conversion of beta-hydroxybutyrate to acetone and acetoacetic acid.

The following biochemical parameters suggest resolution of HHS:

- Plasma effective osmolality (exclude urea in osmolality calculation) below 300 mosmol/kg.
  - Blood glucose <250 mg/dL.
  - Urine output >0.5 mL/kg/h.

  Their cognitive status has improved.

Step 8: Switch to Subcutaneous Insulin When Stable

- Maintain IV insulin until biochemically stable and the patient has taken at least two meals.
- Switch to subcutaneous regular insulin with half dose of total intravenous insulin requirement either as a fixed dose or sliding scale insulin as per protocol.
- IV infusion can be stopped after an overlap of 2 h from the first dose of subcutaneous insulin.
- Total daily dose (TDD) can be calculated using weight-based formula 0.5–0.6 units/kg/day or 0.3 units/kg/day in frail patients, with chronic kidney disease or any risk for developing hypoglycemia.
- Use 40–60% TDD as basal insulin dose and the remaining divided into three mealtime doses of rapid-acting insulin.

- The first dose of basal subcutaneous insulin should be administered before IV insulin is discontinued. Abrupt discontinuation of IV insulin may result in the recurrence of hyperglycemia and ketoacidosis.
- Stop SGLT2 inhibitor treatment during hospitalization.
- Basal-bolus dosing is recommended, and insulin coverage should be round the clock.
- Avoid using ultra-long-acting insulin as a basal insulin (e.g., degludec).

Step 9: Identify Precipitating Factors

- They should be sought and treated. Common precipitants include the following:
- Missed insulin therapy
- Infections—pneumonia, sepsis, and urinary tract infection
- Trauma
- Pancreatitis
- Myocardial infarction
- Pregnancy
- Stroke
- Steroid use

Step 10: Continue Supportive Care

- The urinary catheter: Consider catheterization in persistent hypotension, renal failure, anuria, and impaired consciousness. Maintain strict asepsis during catheterization.
- The central venous pressure (CVP) line: A must-have for all patients who present with shock. Also consider in the elderly with concomitant illness, cardiac failure, or renal failure even in the absence of hypotension.
- Thromboembolic complications are common, and DVT prophylaxis should be initiated.
- The nasogastric tube: If consciousness is impaired, use it to avoid aspiration of gastric contents.
- Appropriate antibiotics if infection is a possible trigger.

Hypoglycemia

A 70-year-old male patient, with type 2 diabetes mellitus, was brought to the emergency department with a history of feeling unwell, nausea, vomiting for 2 days, sudden onset of giddiness, sweating, palpitations, and altered sensorium. Blood glucose on a glucometer was 42 mg/dL.

Impaired consciousness in diabetic patients is most commonly due to hypoglycemia that is most often drug-induced. Symptoms of hypoglycemia are nonspecific, and this can masquerade as cardiorespiratory, neurological, and even psychiatric problems. A low threshold for checking blood sugar in all diabetic patients to exclude hypoglycemia is warranted as it is an imminently treatable condition and if left unattended leads to mortality and severe morbidity.

Step 1: Promptly Identify Clinical Features of Hypoglycemia

- Features of hypoglycemia could be neurogenic such as diaphoresis, tremor, anxiety, palpitation, hunger, paresthesia, and tachycardia caused by sympathetic stimulation.
- These may be absent in patients with autonomic neuropathy or on β-blockers.
- In some patients, neuroglycopenic features such as drowsiness, behavioral abnormalities, coma, and seizures predominate.

Step 2: Check Blood Glucose Immediately

- Urgent capillary sugar should be checked with the bedside glucometer. If possible, a simultaneous venous sample should be sent to the laboratory for glucose analysis.
- Point-of-care glucometers generally overestimate glucose values in the lower range. Whenever hypoglycemia is suspected, always send blood for glucose estimation by glucose analyzer.
- Administration of dextrose should not be delayed if blood glucose checking cannot be done immediately.
- If the blood glucose level is less than 70 mg/dL and symptoms improve with glucose administration, then patient symptomatology may be attributed to hypoglycemia.

Step 3: Give Intravenous Dextrose

- Reverse hypoglycemia rapidly with 50 mL of 25–50% glucose given intravenously.
- Check blood glucose after dextrose infusion and repeat the injection till the glucose is above 70 mg/dL for at least two consecutive readings and the patient is asymptomatic.
- Start intravenous dextrose infusion 6-hourly with frequent blood glucose monitoring in patients on long-acting insulin, oral hypoglycemic drugs, or renal impairment as they are prone to recurrent hypoglycemia.

Step 4: Consider Alternative Agents in Specific Circumstances

- Injection glucagon may be given in a dose of 1 mg intramuscularly or subcutaneously if venous access is not possible.
- Injection octreotide 25–50 mcg may be given subcutaneously or as an intravenous infusion in patients with resistant hypoglycemia, sulfonylurea-induced hypoglycemia, or hypoglycemia induced by drugs like quinine or quinidine.

Step 5: Consider Precipitating Factors of Hypoglycemia in Diabetic Patients

- Missed meals/inadequate food intake
- Insulin overdose
- Change of therapy/dosage of hypoglycemic drugs or insulin
- Concomitant ingestion of drugs causing hypoglycemia
- Presence of hepatic or renal failure

Step 6: Consider Disorders and Drugs Associated with Hypoglycemia (See Tables 8.4 and 8.5)

- In an intensive care unit, certain disorders are associated with hypoglycemia, and frequent blood glucose monitoring should be done in these patients.
- Hypoglycemia is more common if there is intolerance to enteral feeding and the patient is not started on parenteral nutrition.
- Many patients in the ICU have altered mental states and/or are under sedation, and hypoglycemic episodes may remain unnoticed in these patients, so, frequent blood glucose monitoring is essential in these groups of patients.
- Many patients in ICUs are on intravenous insulin infusion. Discontinuation or intolerance to enteral feeding and stopping parenteral nutrition without simultaneously stopping insulin leads to hypoglycemia.
- At lower glucose range and in low perfusion states, bedside glucometer loses its accuracy.

Table 8.4 Common causes of hypoglycemia in the ICU

Insulin
Oral hypoglycemic agents
Sepsis (including malaria)
Hepatic failure
Alcohol
Adrenal crisis (including steroid withdrawal)
Drugs

Table 8.5 Drugs associated with hypoglycemia

Insulin
Oral hypoglycemic agents
Gatifloxacin
Quinine
Artesunate derivatives
Pentamidine
Lithium
Propoxyphene

Suggested Reading

Dhatariya KK, Joint British Diabetes Societies for Inpatient Care. The management of diabetic ketoacidosis in adults—an updated guideline from the Joint British Diabetes Society for Inpatient Care. Diabet Med. 2022;39:e14788.

Gosmanov AR, Gosmanova EO, Dillard-Cannon E. Management of adult diabetic ketoacidosis. Diabetes Metab Syndr Obes. 2014;7:255–64. Published 2014 June 30. https://doi.org/10.2147/DMSO.S50516.

Hillman K. Diabetic ketoacidosis and hyperosmolar nonketotic coma. In: Albert RK, Slutsky A, Ranieri M, Takala J, Torres A, editors. Clinical critical care medicine. Philadelphia: Mosby Inc; 2006. p. 507–15.

Magee MF, Bhatt BA. Management of decompensated diabetes. Diabetic ketoacidosis and hyperglycemic hyperosmolar syndrome. Crit Care Clin. 2001;17(1):75–106.

Umpierrez GE, Davis GM, ElSayed NA, Fadini GP, Galindo RJ, Hirsch IB, et al. Hyperglycemic crises in adults with diabetes: a consensus report. Diabetes Care. 2024;47(8):1257–75. https://doi.org/10.2337/dci24-0032. *A recent consensus guideline*

Viallon A, Zeni F. Does bicarbonate therapy improve the management of severe diabetic ketoacidosis? Crit Care Med. 1999;27(12):2690. *Data from the literature and this study are not in favor of the use of bicarbonate in the treatment for diabetic ketoacidosis with pH values between 6.90 and 7.10*

Zhong VW, Juhaeri J, Mayer-Davis EJ. Trends in hospital admission for diabetic ketoacidosis in adults with type 1 and type 2 diabetes in England, 1998–2013: a retrospective cohort study. Diabetes Care. 2018;41:1870–7.

Part II

Oncology and Blood Disorders

Transfusion Practices and Complications

9

Nayana Amin and Vijaya Patil

Case Vignette

A 40-year-old man with polytrauma was admitted with multiple long bone fractures, thigh hematoma, and bleeding profusely from a lacerated wound. He looks pale and diaphoretic. Pulse 120/min, BP 90/50.

Blood transfusion is a common practice in the ICU with an estimated 40% of patients having a transfusion. It is generally safe but occasionally may lead to minor or life-threatening consequences if attention to detail and protocol is not met during transfusion.

Step 1: Resuscitate

- Secure two large-bore (14G/16G) IV cannulae.
- Send blood for grouping, cross-matching, complete blood count (CBC), coagulation profile, and other appropriate investigations.
- Proper coordination with the blood bank is mandatory in these situations for early and proper acquisition of blood products.

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Step 2: Transfuse Packed RBCs or Blood Components (Tables 9.1 and 9.2)

- If the patient is bleeding profusely and hemodynamically unstable, use group-specific uncross-matched blood or O Rh-negative packed cells while waiting for cross-matched blood.

Table 9.1 Alternative red blood cell products

Technique	Purpose	Indications	Comments
Leukoreduction	Minimize the risk of cytomegalovirus transmission Reduces febrile nonhemolytic transfusion reactions (FNHTR) and alloimmunization	High-risk immunocompromised patients, patients needing multiple transfusions, patients who have had FNHTR	Does not prevent TA-GVHD (transfusion-associated graft vs. host disease)
Separate types of filters to allow for RBC and platelet passage only, ideally should be used during collection but may be used during transfusion			
Washed RBCs	Prevent allergic reaction Reduce the risk of hyperkalemia Anti-IgA antibody	Recurrent severe allergic reactions despite premedication, IgA-deficient patients, patients at risk of hyperkalemia	Not equivalent to leukoreduction, 15–20% loss of RBCs
RBCs washed with saline to remove >98% of plasma proteins, antibodies, leukocytes, and electrolytes			
Gamma irradiation to inactivate leukocytes	Prevents TA-GVHD	Premature infants, patients with malignancy, recipients of allogenic hemopoietic transplants, transfusion to blood relatives	Does not reduce infectious risks or FNHTR
Frozen RBCs	For individuals with rare blood group		
Whole blood	Massive blood transfusion		
Packed red blood cells (PRBCs)	Reduces transfusion-associated circulatory oerload (TACO)		
CMV-negative RBC	For immunosuppressed patients patients at risk of CMV infection		

Table 9.2 Blood components and antifibrinolytics

Product	Content	Indications	Dose	Caution	Expected correction
FFP (fresh frozen plasma)	All coagulation factors in normal concentration and plasma proteins	Deficiencies and consumption of coagulation factors	15 mL/kg	Should be group-specific	15 mL/kg of FFP will increase coagulation factor concentration by 25–30%, which is enough for adequate clotting
	Thawed plasma may be stored (1–6 °C) for up to 5 days	Reversal of vitamin K antagonists (VKA), e.g.. warfarin		Thawed plasma should be transfused within 24 h if kept at room temperature	
		Massive blood transfusion (>1 blood volume within several hours)		Use blood filters	
		Replacement in plasmapheresis for any indication			
		Raised INR and planned invasive procedure			
Cryoprecipitate	Fibrinogen VIII/vWF (von Willebrand's factor), factor XIII, and fibronectin	Decreased fibrinogen, liver disease, post-thrombolysis bleeding	1 unit/7–10 kg body weight	Should be transfused within 6 h of thawing Does not have to be group-specific as the volume of plasma is less	1 unit cryoprecipitate/10 kg body weight
				Use blood filters	Raises plasma fibrinogen concentration by ~50 mg/dL

(continued)

Table 9.2 (continued)

Product	Content	Indications	Dose	Caution	Expected correction
Platelet	Random donor platelets—approximately 8.0 × 10^{10} platelets with 50 mL plasma	Bleeding due to critically decreased circulating platelet counts or functionally abnormal platelets	Infused over 30–60 min	Should be group specific	Expect an adult platelet count increment of ~7000–10,000/mm^3 for each RDP (random donor platelet) given or 30,000–60,000/mm^3 for each SDP (single donor platelet) given
	Single donor platelets—3.5–4.0 × 10^{11} platelets with 250 mL plasma Requires pheresis to collect	Maintain platelet count >10,000/mm^3 in stable nonbleeding patients, >30,000/mm^3 in unstable nonbleeding patients, and >50,000/mm^3 in patients undergoing invasive procedures or actively bleeding >100,000/mm^3 or for CNS trauma		Do not refrigerate	In pediatrics, a dose of 5–10 mL/kg of platelets (RDP or SDP) should result in 50–100,000/mm^3 increment
Desmopressin	Stimulate the endothelial release of factor VIII and vWF into the plasma (V2 receptor-mediated effect), where they form a complex with platelets and enhance their ability to aggregate	Hemophilia A, von Willebrand's disease, uremic thrombocytopathy	0.3mcg/kg repeated as clinically necessary at intervals of 12–24 h	Tachyphylaxis may occur after three or four doses	

Prothrombin complex concentrate (PCC)	Prepared by ion-exchange chromatography process from the cryoprecipitate supernatant of large plasma pools after removing antithrombin and factor XI. 2 types of PCC 3 factor (contains factors II, IX, and X) 4 factor (contains factors II,VII, IX, and X)	Urgent reversal of VKA, Reversal of direct oral anticoagulants (DOAs) if specific antidote is not available Congenital deficiency of vitamin-K-dependent clotting factors (off label) Massive transfusion (off label)	INR: 2–4: 25 U/kg; maximum dose: 2500 U INR: 4–6: 35 U/kg; maximum dose: 3500 U INR: > 6: 50 U/kg; maximum dose: 5000 U	Allergic reactions Thromboembolic complications	
Activated factor VIIa		Approved indications: factor VIIa deficiency, hemophilia A and B, acquired haemophilia, Glanzmann thrombasthenia, off off-label indications—trauma and surgery where bleeding continues inspite of conventional treatment	30 up to 90 mcg/kg Intravascular half-life is <2 h and hence repeat every 2–3 h till satisfactory hemostasis is achieved		Target trough activity of at least 10–15 IU% (10–15%) is needed
Antifibrinolytic drugs					
Epsilon-aminocaproic acid	Competitive inhibitor of plasminogen activation	Situations associated with hyperfibrinolysis such as operations requiring cardiopulmonary bypass, liver transplantation, and some urological and orthopedic operations	100 mg/kg as an IV bolus followed by an infusion of 15 mg/kg/h (max 24 gm/day)		

(continued)

Table 9.2 (continued)

Product	Content	Indications	Dose	Caution	Expected correction
Tranexamic acid	Competitive inhibitor of plasminogen activation		Bolus dose of 10–15 mg/kg IV followed by 1 mg/kg/h for 5–8 h		
Aprotinin	Powerful inhibitor of plasmin, trypsin, chymotrypsin, kallikrein, thrombin, and activated protein C	Cardiac surgery, major orthopedic surgeries, liver transplant	Loading dose of two million international unit followed by continuous infusion of 500,000 KIU/h		

- Full cross-matching process usually takes 1 h and detects all clinically significant antibodies. In emergency bleeding conditions, one can also ask for immediate spin that detects major ABO incompatibility and the presence of a "cold" or room temperature reactive antibody.
- In hemodynamically stable patients, use group-specific cross-matched blood. There is no advantage of using fresh blood over old blood (within the stipulated shelf life of 42 days).
- In the presence of major active bleeding, transfuse blood rapidly over 30 min (if available, use the rapid infusion pump, which can give fluids at a faster rate).
- 4 mL/kg of packed RBCs (usually one unit) increases the hemoglobin by 1 g/dL and hematocrit by 3% in the absence of active bleeding.
- Rate of transfusion can be adjusted as per need, that is, rapidly in hypovolemic patients and slowly in stable patients; however, once issued from the blood bank, blood transfusion should be over within 4 h to prevent the growth of organisms. If blood cannot be transfused fully within this time, it is advisable to discard it.
- Transfuse blood and blood products through the filter to prevent the passage of small clots that may form in stored blood.
- The filter with a pore size of 170–200 μm is recommended for routine transfusions of RBCs, platelets, fresh frozen plasma (FFP), and cryoprecipitate.
- Filters with smaller pore sizes are more efficient, but they would increase resistance and filter out platelet aggregates, reducing the efficiency of transfused platelets.
- Microaggregate filters with 20–40 μm size are recommended during cardiopulmonary bypass only.
- Filters can slow down the rate of blood transfusion. So, the standard recommendation is to use a new set for every transfusion. In case of rapid transfusion if the filter does not look clogged, change the set every two transfusions.
- Use fluid warmer to transfuse blood in massive blood loss. This helps prevent hypothermia, which can contribute to the coagulopathy by causing reversible platelet dysfunction, altering coagulation kinetics, and enhancing fibrinolysis.
- Hypothermia also causes ventricular dysrhythmias and citrate toxicity due to reduced citrate metabolism.
- Do not use unconventional and uncontrolled methods for blood warming such as keeping near heat source or immersing the bag in hot water bath.

Step 3: Correct Coagulopathy

- Correct high INR with FFP/PCC and low platelets with platelet transfusions only in an actively bleeding patient.
- Do not correct raised INR prophylactically in a nonbleeding patient unless surgical intervention is contemplated.
- Prophylactic use of platelets before central venous catheter placement in patients with thrombocytopenia was recently studied There were more bleeding events I

patients who were not transfused prophylactically with a platelet count of 10,000–50,000/cu mm.
- Other coagulopathic abnormalities need to be corrected.
- Antifibrinolytic agents may be used to minimize bleeding in situations like trauma.
- Correct hypothermia.
- Normalize calcium.
- Consider activated factor VII in specific situations such as hemophilia A and B and congenital factor VII deficiency. It may be beneficial in trauma and surgical hemorrhages when hemorrhage has not responded to conventional therapy (off-label use)
- Use thromboelastography (TEG) or rotational thromboelastometry (ROTEM) if available to further guide the transfusion strategy.

Step 4: Control the Source of Bleeding

- Investigate to find out the source of bleeding and consider options available for controlling the bleeding (interventional radiology or surgery).
- Urgent consultation is required if needed with these specialties.

Step 5: Assess the Severity of Bleeding

- Massive blood loss may be defined as
  - Loss of one blood volume within a 24-h period
  - Loss of blood equivalent to 7% of lean body weight in an adult (5 L) and 8–9% in a child
  - Loss of 50% of blood volume within 3 h
  - Loss of blood at a rate over 150 mL/min

Step 6: Manage Massive Blood Loss

- Institute continuous invasive pressure monitoring for fluid management in the presence of ongoing bleeding.
- Collect blood samples for cross-matching of further blood and blood products. Serial CBC (Hb and platelets) and coagulation tests (prothrombin time, APTT, and fibrinogen), blood gas analysis, serum electrolytes (Na, K, Mg, ionized calcium), and serum lactate should be done.
- These should be repeated frequently in ongoing bleeding and after every component therapy.
- Transfusion of platelets, FFPs, and cryoprecipitate should be guided by laboratory results or point-of-care testing.

- FFP administration should begin after the loss of one blood volume and platelets after a loss of 1.5 times the blood volume.
- 1:1:2 ratio should be maintained for packed RBCs, FFP, and random donor platelets to prevent dilutional coagulopathy and dilutional thrombocytopenia due to massive blood transfusion, which results in a vicious cycle of bleeding diathesis.
- Cryoprecipitate is prepared by rapid thawing of FFP, thus fibrinogen content is the same in one unit of FFP and one unit of cryo. The only advantage of cryo is smaller volume. In ongoing blood loss, patients do need volume, and since FFP also contains plasma, it will be preferable in ongoing blood loss.
- Administer cryoprecipitate if fibrinogen is less than 100 mg/dL and there is a fear of volume overload by use of FFP.
- One can also consider fibrinogen concentrate (available in our country) for hypofibrinogenemia at 70 mg/kg.
- If patients with A or B blood group have received multiple units of O Rh-positive whole blood, then they can be switched back to their inherent group-specific blood only after subsequent testing by the blood bank indicates it is safe to do so.

Step 7: Identify and Manage Transfusion-Induced Complications (Table 9.3)

- Stop blood transfusion immediately if any acute hemolytic transfusion reaction is suspected.
- Hypotension may be due to acute ongoing hemorrhage, acute severe transfusion reaction, allergic reaction/anaphylaxis, or rarely due to septic shock (due to transfusion of blood with bacterial contamination).
- Check the identity of the recipient with the details on the bag and the cross-match form.

Table 9.3 Transfusion-related complications

Reaction	Cause	Clinical signs	Treatment
Febrile nonhemolytic transfusion reaction (FNHTR)	Reaction between the recipient's leukocyte antibodies (formed due to previous transfusions or pregnancies) and transfused leukocytes. Pyrogenic cytokines released from the leukocytes in stored blood.	Fever is a main sign, can also get chills, rigors, tachypnea, headache	Give paracetamol and resume transfusion at a slow rate
Allergic reaction	Reaction to soluble allergens in the donor's plasma.	Urticaria, flushing, pruritus	Give 10 mg IV chlorpheniramine maleate and resume transfusion

(continued)

Table 9.3 (continued)

Reaction	Cause	Clinical signs	Treatment
Anaphylaxis	IgA-deficient individuals react to IgA in transfused units.	Flushing, pruritus, laryngospasm, bronchospasm	Stop transfusion Supplement O_2 SC/IV epinephrine, 100 mg IV hydrocortisone, 10 mg IV chlorpheniramine maleate Salbutamol nebulization IV fluids Send the blood back to the blood bank along with a sample of the patient’s blood Use washed RBCs in future
Sepsis	Bacterial contamination of blood and blood products, Yersinia, malaria.	Fever, chills, hypotension	Stop transfusion Contact the blood bank and send the remaining blood to the blood bank Send blood culture
Acute hemolytic transfusion reaction (<24 h)	Immune-mediated—due to mismatch or incompatibility of the recipient with the donor products. The usual incompatibility is blood group system ABO. However, there can also be reactions with other “minor” antigens such as Duffy and Kell.	Fever, chills, flushing, chest pain, back pain, vomiting, tachycardia, hypotension	Stop transfusion Reconfirm the patient’s identity and blood group Inform the blood bank and return blood to the blood bank Send blood for CBC, coagulation profile, direct Coombs’ test, peripheral smear for evidence of hemolysis Oxygen supplementation if needed Infuse IV fluids to maintain urine output >100 mL/h Can consider diuretics if urine output falls Treat DIC with appropriate components

(continued)

Table 9.3 (continued)

Reaction	Cause	Clinical signs	Treatment
Delayed hemolytic transfusion reaction (24 h to 28 days)	Nonimmune-mediated—transfusion of damaged red cells.	Malaise, fever, jaundice, anemia	Conservative management
Transfusion-associated graft-versus-host disease (TA-GVHD) 2–30 days after transfusion	Donor lymphocytes initiate an immune attack against the recipient's cells.	Fever, skin rash, liver dysfunction, diarrhea, severe pancytopenia	No treatment Prevention by using gamma-irradiated blood products in high-risk patients
TACO	Volume overload.	Dyspnea, rales, normal or high BP, desaturation, raised central venous pressure (CVP)/JVP	O_2 supplementation, diuretics, ventilatory support SOS
TRALI	Antibodies in the donor's blood react with neutrophil antigen in the recipient.	Dyspnea, rales, normal or low BP, desaturation, normal or low CVP	Supportive management Ventilate according to acute respiratory distress syndrome network protocol Steroids not indicated

- Transfusion-associated circulatory overload (TACO) is circulatory overload following transfusion of blood or blood product.
- Transfusion-associated acute lung injury (TRALI) is defined as a new acute lung injury (with hypoxemia and bilateral infiltrates on a chest radiograph but no evidence of left atrial hypertension) occurring during or within 6 h after a transfusion, with a clear temporal relationship to the transfusion, and not explained by another acute lung injury (ALI) risk factor.
- Transfusion-related hyperkalemia is more likely to happen in massive trauma, renal failure, and newborn/infants.
- Increased risk of citrate toxicity in massive transfusion in patients with liver disease.

Step 8: Use less Allergenic Blood Products

- In patients with multiple blood transfusions and transfusion-related complications, alternatively processed blood products should be considered (Table 9.1).

Step 9: Consider the Threshold for Blood Transfusion

- If the bleeding has stopped and there are no clinical signs of hypoperfusion, do not transfuse any more blood or blood products.
- In the absence of active bleeding, keep a transfusion threshold of 7.0 gm/dL and 7–8 g/dL Hb in critically ill patients who are hemodynamically stable.
- In the presence of active bleeding, keep higher transfusion threshold of 9–10gm% and further guide by clinical needs.
- Adult critically ill medical and surgical patients suspected to have sepsis and septic shock, during the first 6 h of resuscitation one may consider higher transfusion threshold of 8–10 g/dL.
- Transfusion threshold should be individualized depending on patient age, hemodynamic stability, cardiac status, and availability of group-specific blood.
- RBC transfusion may be beneficial in anemic patients with acute coronary syndrome (keep Hb >9 g/dL).
- For patients undergoing cardiovascular surgery or orthopedic surgery, blood transfusion is to be given to maintain hemoglobin 7–8 g/dL.
- All RBC transfusions in nonbleeding stable patients should be ordered as single units. Obtain post-transfusion Hb before ordering additional units.

Step 10: Use Blood Products Judiciously

- In the absence of bleeding, do not correct high INR with FFP.
- Patients having inadequate intake or on anticoagulants and broad-spectrum antibiotics are likely to have vitamin K deficiency, which can cause deranged INR. They will benefit from intravenous vitamin K supplementation.
- Consider judicious use of intravenous iron and erythropoietin where indicated to minimize need for blood transfusion.

Step 11: Follow the Blood Transfusion Protocol

- Take informed consent.
- Check patient identification, match the unit to be transfused with patient name and hospital registration number, and document the same.

- Perform visual inspection of the blood to be transfused for features of hemolysis.
- Continuous monitoring of the patient during transfusion and respond immediately if any adverse events occur.
- Use only 0.9% normal saline or albumin, ABO-compatible plasma through the same intravenous tubing.
- Initial infusion rate 1–2 mL/min for the first 15 mins to look for any features of hemolytic or allergic reaction.
- Complete transfusion not exceeding 4 h.
- If needed, a post-transfusion hemoglobin may be checked as soon as 15 mins after transfusion.
- Report any adverse reaction.

Case Vignette

A 48-year-old woman with a prosthetic mitral valve on warfarin presents to the emergency department with severe bleeding per vagina for last 12 h. She is pale with cold peripheries, rapid thread pulse, and tachypnea. Her Hb is 5.0 gm% and INR is 7.5.

Follow steps 1 and 2 similar to the first case

Step 3

- Stop warfarin, give 1–2 mg vitamin K IV over 15–20 minutes that will reverse the effect of warfarin in 4–6 h, and use FFP/cryo/PCC for uncontrolled bleeding. Monitor INR 6–8 hourly.
  - American College of Cardiology/American Heart Association guidelines recommend against high-dose (10 mg) vitamin K in patients with mechanical heart valves as this may create a hypercoagulable state with the risk of valve thrombosis. In addition, high dose of vitamin K may lead to warfarin resistance due to the accumulation of vitamin K in the liver.
  - 10 mg vitamin K IV is recommended only when there is no plan for restarting anticoagulation within the next week.
- If there is life-threatening bleeding or bleeding in critical areas (CNS, pericardium, or airways), stop warfarin and correct coagulopathy with FFPs/cryoprecipitate or 4F-PCC.
- Consider supportive measures and give reversal agents whenever indicated. Use appropriate laboratory tests to determine the drug levels (Table 9.4).

Table 9.4 Various anticoagulant agents and their antidotes

Drug	Laboratory tests to determine drug levels	Treatment	
		Minor bleeding	Major bleeding
Unfractionated heparin	Activated partial thromboplastin time (aPTT)		IV protamine 1 mg/100 units of heparin
Low molecular weight heparin (LMWH)	Anti-factor Xa levels		IV protamine 1 mg/100 units dalteparin/tinzaparin or 1 mg protamine/1 mg enoxaparin dose received in the previous 8 h Consider rFVIIa for critical bleeding
Vit K antagonist (warfarin)	Prothrombin time (PT)/ international normalized ratio (INR)	**If INR < 4.5** No bleeding—withhold warfarin till INR is in therapeutic range **If INR 4.5–10** No bleeding—hold warfarin, consider vitamin K 2.5 mg PO Urgent reversal—give vitamin K 1 mg IV **If INR > 10** No bleeding—hold warfarin, give vitamin K 2.5 mg PO or 1–2 mg IV over 30 mins; repeat every 24 h Urgent reversal—give vitamin K 1–2 mg IV over 30 mins, repeat every 6–24 h	Discontinue oral anticoagulant (OAC) 5–10 mg IV vitamin K 4F-Prothrombin complex concentrates (4F-PCC) **If INR 1.5–3.9**, give 25 units/kg 4F-PCC max of 2500 units **If INR 4–6**, give 35 units/kg 4F-PCC max of 3500 units **If INR > 6**, give 50 units/kg 4F-PCC max of 5000 units If 4F-PCC not available give FFP at 10–15 mL/kg Activated prothrombin complex concentrate (aPCC) is not indicated
Direct thrombin inhibitors Dabigatran	TT—dilute thrombin time ECT—ecarin clotting time ECA—ecarin chromogenic assay If the above tests are not available then Thrombin time aPTT		IV idarucizumab or IV 4 PCC/(aPCC) at 50 units/kg No role of FFP Anticoagulant discontinuation Antifibrinolytic agent (tranexamic acid) Consider activated charcoal if drug has been ingested within 2–4 h

(continued)

Table 9.4 (continued)

Drug	Laboratory tests to determine drug levels	Treatment	
		Minor bleeding	Major bleeding
Oral factor Xa inhibitors Rivaroxaban, epixaban, and endoxaban	Anti-factor Xa levels Normal aPTT does not exclude significant drug levels Normal PT indicates complete clearance of Xa inhibitor PT and aPTT not sensitive for epixaban		Andexanet alfa if available IV 4 PCC/aPCC at 50 units/kg Anticoagulant discontinuation Antifibrinolytic agent (trenexemic acid) Consider activated charcoal if drug has been ingested within 2–4 h No role of FFP

Suggested Reading

BCSH. Guidelines for management of massive blood loss. Br J Haematol. 2006;135:634–41. *It is an evidence-based guideline on the management of massive blood loss*

Cooper DJ, ZK MQ. Age of red cells for transfusion and outcomes in critically ill adults. N Engl J Med. 2017;377(19):1858–67. *Critically ill adults received randomly either the freshest available, compatible, allogeneic red cells (short-term storage group) or standard-issue (oldest available), compatible, allogeneic red cells (long-term storage group). The primary outcome was 90-day mortality. Among the 2457 patients in the short-term storage group, the mean storage duration was 11.8 days. Among the 2462 patients in the long-term storage group, the mean storage duration was 22.4 days. At 90 days, there were 610 deaths (24.8%) in the short-term storage group and 594 (24.1%) in the long-term storage group P=0.57). The age of transfused red cells did not affect 90-day mortality among critically ill adults*

Klein HG, Spahn DR. Series on transfusion medicine. Lancet. 2007;370:415–48. *An excellent review on red cell transfusion, platelet transfusion, and coagulation factor concentrates*

Lacroix J, Hébert PC. Age of transfused blood in critically ill adults. N Engl J Med. 2015;372(15):1410–8. *1211 patients were randomly assigned to receive fresh red cells and 1219 patients were assigned to receive standard-issue red cells Red cells were stored a mean (±SD) of 6.1±4.9 days in the fresh-blood group as compared with 22.0±8.4 days in the standard-blood group (P<0.001). At 90 days, 448 patients (37.0%) in the fresh-blood group and 430 patients (35.3%) in the standard-blood group had died which was not significant . Transfusion of fresh red cells compared with standard-issue red cells did not decrease the 90-day mortality among critically ill adults*

Napolitano LM, Kurek S, American College of Critical Care Medicine of the Society of Critical Care Medicine, Eastern Association for the Surgery of Trauma Practice Management Workgroup. Clinical practice guideline: red blood cell transfusion in adult trauma and critical care. Crit Care Med. 2009;37:3124–57. *These are evidence-based guidelines on the use of RBC transfusions in adult trauma and critical care endorsed by SCCM* van Baarle FLF, van de Weerdt EK, van der Velden WJFM, et al. Platelet transfusion before CVC placement in patients with thrombocytopenia. N Engl J Med. 2023;388(21):1956–65. *Large RCT on prophylactic platelet transfusion*

Yazer MH, et al. How do I implement a whole blood program for massively bleeding patients? Transfusion. 2018;58(3):622–8. *A review article on practical implementation of blood transfusion in massive bleeding*

Websites

2017 ACC Expert Consensus Decision Pathway on Management of Bleeding in Patients on Oral Anticoagulants: A Report of the American College of Cardiology Task Force on Expert Consensus Decision Pathways. J Am Coll Cardiol. 2017;70(24):3042–3067

www.asahq.org/publicationsAndServices/transfusion.pdf

www.bcshguidelines.com

www.transfusionguidelines.org.uk

Disseminated Intravascular Coagulation and Thrombocytopenia

10

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Case Vignette
A 40-year-old male patient was admitted with acute pancreatitis. He developed fever, tachycardia, hypotension, and respiratory distress on the third day of admission. His abdomen was severely tender and distended. The next morning the nurse noticed excessive oozing from arterial and central line insertion sites, and his abdomen was further distended.

Bleeding manifestation due to disseminated intravascular coagulation (DIC) occurs in 1% of hospital admission. Assessing and managing these patients require a systematic approach as DIC is a reflection of underlying systemic disease affecting the coagulation system, resulting in procoagulant activation, fibrinolytic activation, consumption coagulopathy, and end-organ damage, which needs to be recognized and treated.

Step 1: Initial Resuscitation

- Special emphasis should be placed on stabilizing hemodynamics, and if needed, blood and blood product transfusion should be started.
- Care should be taken in establishing venous access in actively bleeding patients who may be coagulopathic.

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- Peripheral access is preferable to central.
- In case of central venous access, use ultrasound-guided venous cannulation if possible and preferably choose compressible sites like the internal jugular or femoral vein.
- Avoid arterial punctures.

Step 2: Take Relevant History and Perform Focused Physical Examination

- Take history of known systemic conditions associated with DIC and coagulation disorders (Table 10.1).
- Review the drug history, particularly the use of direct oral anticoagulants (DOACs), heparin, and warfarin, and consumption of antiplatelet agents, including nonsteroidal anti-inflammatory drugs.
- Look for bleeding manifestation, superficial like skin and mucosal (petechiae, purpura) or visceral and deep-seated (gastrointestinal bleeding).
- Look for thrombotic manifestations like deep vein thrombosis (DVT) of the lower limbs or venous or arterial thrombosis at any other site (e.g., cerebral).
- Differential diagnosis includes severe liver disease, heparin-induced thrombocytopenia, microangipathic hemolytic anemia, and hemophagocytic syndrome (HLH).

Table 10.1 Conditions associated with DIC

Infections	Bacterial—Gram-negative and Gram-positive sepsis
	Viral—cytomegalovirus, HIV, hepatitis, dengue
	Fungal
	Parasitic—malaria, leptospirosis
Malignancy	Solid tumors
	Hematological—acute promyelocytic leukemia is commonly associated with DIC
Obstetric	Amniotic fluid embolism
	Placenta abruption
	Preeclampsia
	Intrauterine fetal death/retained products of conception
Toxic and immunological insults	Viper snake bites
	Massive transfusion
	ABO transfusion incompatibility
	Transplant rejection
Massive inflammation	Severe trauma
	Crush injuries
	Massive burns
	Fulminant liver failure
	Severe hypo−/hyperthermia
	Severe pancreatitis
Vascular disorders	Aortic aneurysms
	Giant hemangiomas

Step 3: Investigate to Ascertain the Type and Cause of Bleeding (Table 10.2)

Table 10.2 Coagulation profile

Test	What does it monitor	Normal value	Inference
Prothrombin time	Factors that are in the extrinsic pathway and common pathway: factors VII, X, V, and II	11–13 s	Prolongation of the PT is most often a result of deficiencies in factor VII but can also be caused by any of the extrinsic and common pathway factors. Decreased fibrinogen, levels less than 100 mg/dL will also prolong the PT.
			Cholestatic jaundice.
			Acute or chronic liver failure.
			DIC.
			Malabsorption.
			Vitamin K deficiency.
			Coumadin (warfarin) therapy.
			Factors I, II,V, VII, X deficiency.
Activated partial thromboplastin time	Factors that are designated in the intrinsic pathway: factors XII, XI, IX, VIII, X, V, II, and fibrinogen	28–34 s	Heparin therapy.
			Factor deficiency.
			Presence of an inhibitor like lupus anticoagulants.
Platelet count	Quantifies platelet number	130–400 × 10^9/L	Decreased production (bone marrow disorder), increased destruction, idiopathic thrombocytopenic purpura (ITP), thrombotic thrombocytopenic purpura, sequestration (hypersplenism).
Thrombin time	Evaluate the last step of coagulation (conversion of fibrinogen to fibrin)	13–15 s	Heparin therapy.
			DIC.
			Qualitative fibrinogen abnormalities or hypofibrinogenemia.
			Elevated fibrin degradation products (FDPs).
Fibrinogen level		200–500 mg/dL	Congenital and acquired hypofibrinogenemia.
			DIC.
D-dimer	Cross-linked D fragments of the protein fibrinogen	500 ng/mL	Deep venous thrombosis, DIC, pulmonary embolism, thrombolytic treatment, postoperative.
Antithrombin (AT), protein C	Anticoagulant activity	65–135 IU/dL	Liver dysfunction, capillary leak syndrome.
Plasmin–plasmin inhibitor complex	Antifibrinolytic	0.8 μg/dL	Venous thromboembolism, post-surgery.

- Complete blood count, including platelet count and peripheral smear, for the presence of fragmented RBCs.
- Prothrombin time (PT), activated partial thromboplastin time (APTT), and thrombin time (TT).
- Fibrinogen level, fibrin degradation product (FDP), and D-dimer.
- Renal and liver function tests.
- The commonest laboratory abnormality is thrombocytopenia followed by elevated FDPs, prolonged PT, prolonged APTT, and a low fibrinogen.
- D-dimer, FDP, and antithrombin levels can be used for rapid and specific diagnosis of DIC, with antithrombin providing an indicator for severity and prognosis.
- Diagnosis of DIC is essentially confirmed by demonstrating increased thrombin generation (decreased fibrinogen) and increased fibrinolysis (elevated D-dimer or FDP).

Step 4: Ascertain Severity and Prognosticate Outcome

- Calculate the DIC score (Table 10.3) with the International Society of Thrombosis and Haemostasis (ISTH) scoring system that provides objective measurement of DIC and correlates with outcome.

Table 10.3 Scoring systems for DIC

	ISTH criteria	JMWH criteria	JAAM criteria
Clinical condition predisposing to DIC	Essential	1 point	Essential
The presence of clinical symptoms	Not used	Bleeding—1 point Organ failure—1 point	SIRS score ≥ 3—1 point
Platelet count (× 10^9/L)	50–100 —1 point <50—2 points	80–120—1 point 50–80—2 points < 50—3 points	80–120 or > 30% reduction—1 point < 80 or > 50% reduction—2 points
Fibrin-related marker	Moderate increase—2 points Marked increase—3 points	FDP (μg/mL) 10–20—1 point 20–40—2 points > 40—3 points	FDP (μg/mL) 10–25—1 point > 25—3 points
Fibrinogen	<1 g/L—1 point	1–1.5 g/L—1 point < 1 g/L—2 points	
PT	Prolongation 3–6 s—1 point > 6 s —2 points	PT ratio 1.25–1.67—1 point > 1.67—2 points	PT ratio ≥ 1.2—1 point
DIC diagnosis	**≥ 5 points**	**≥ 7 points**	**≥ 4 points**

ISTH International Society of Thrombosis and Haemostasis, *JAAM* Japanese Association for Acute Medicine, *JMWH* Japanese Ministry of Health and Welfare

Step 5: Continue Resuscitation

- Continue resuscitation and maintain hemodynamic stability using crystalloids.
- Avoid colloids as they interfere with clotting.
- If colloids are used at all, use gelatin, or if you are using starches, use tetrastarch preferably as they have less effect on the coagulation profile, but do not exceed the maximum dose (50 mL/kg/day).

Step 6: Correct Coagulopathy

- Repeat the coagulation profile and complete blood count frequently and replace blood and blood products.
- Rotation thromboelastometry (ROTEM) or thromboelastography (TEG) can be used to guide blood product administration while managing DIC.
- In the presence of ongoing blood loss, try to normalize prothrombin time and APTT and aim to maintain a platelet count of more than 50,000.
- Do not prophylactically transfuse platelet or plasma as long as platelet count is above 10,000/cu.mm.
- Do not use antifibrinolytic agents as they may aggravate thrombosis.
- Patients who have DIC with a primary hyperfibrinolytic state (obstetrical patients, prostatic surgery) and who have severe bleeding can be treated with lysine analogs, such as tranexamic acid (e.g., 1 g every 8 h).
- There is no role of heparin in actively bleeding patients.
- Heparin should be considered only where thrombosis predominates such as arterial or venous thromboembolism or severe purpura fulminans associated with vascular skin infarction.
- Use of prothrombin complex concentrates (PCC) has been shown to increase the risk of thromboembolic complications, especially with high or repeated doses. It should be only used in patients where FFP transfusion is not possible and patient is actively bleeding in critical areas

Step 7: Treat the Underlying Disorder

- Repeat the tests to monitor the dynamically changing scenario and continue treatment based on clinical observation and laboratory results.
- Once the patient stops bleeding, do not try to correct laboratory abnormalities as transfusion of blood and blood products should be based on clinical condition and bleeding rather than laboratory values only.

Calculate Score

- More than five overt DIC: repeat score daily.
- Less than five suggestive for nonovert DIC: repeat for the next 1–2 days.

- Chronic DIC is associated with malignancy (especially gastric, pancreatic, ovarian, or brain tumors). There may be venous or arterial thromboembolism, mild or no thrombocytopenia, mild abnormalities of PT, PTT, fibrinogen, and d-dimer.

Thrombocytopenia

A 50-year-old male patient was admitted with acute pancreatitis. His blood investigations showed Hb 10.7 g%, WBC 12,000/mm^3, and platelets 110,000/mm^3. On the third day, he worsened clinically. His WBC count was 20,000/mm^{3}and platelets were 70,000/mm^3. However, the next day, he further deteriorated, requiring inotropes and ventilatory support. His Hb dropped to 6.4 g%, his WBC count rose to 28,000 mm^3, and platelets further dropped to 40,000/mm^3.

Step 1: Resuscitate

- Resuscitate, monitor, and stabilize in the ICU (refer Chap. 24). In patients with low platelets and coagulopathy, ultrasound-guided jugular venous catheter insertion for fluid resuscitation should be performed.
- Send blood for peripheral blood smear, grouping, cross-matching, coagulation profile, and biochemistry.

Step 2: Assess the Severity of Thrombocytopenia

- Thrombocytopenia is defined as a platelet count less than 150×10^9/L.
- In critically ill patients, a threshold of less than100×10^9/L may be taken.
- The ability to form a hemostatic plug is retained until the platelet count drops to less than 100×10^9/L.

Step 3: Assess the Cause of Thrombocytopenia (Table 10.4)

- Careful history, physical examination, previous medical records, and current chart review usually reveal the cause of low platelet count.
- Ask about bleeding from other sites in the past, for example, frequent nosebleeds, gum bleeds, melena, hemoptysis, and blood in stool or urine.
- History of previous platelet counts.
- History of previous blood or platelet transfusion.

Table 10.4 Causes of thrombocytopenia

Pseudothrombocytopenia seen in asymptomatic patients	EDTA causes in vitro clumping of platelets. Presence of platelet clumps in the peripheral smear and a normal repeat platelet count in citrated blood confirm pseudothrombocytopenia. In some patients, automated blood reports show thrombocytopenia due to the presence of giant platelets that are counted as RBCs in automated machines; however, manual platelet count is normal.
Dilutional thrombocytopenia	Massive blood transfusion.
Ambulatory patients	ITP
	Drug-induced—chemotherapy, miscellaneous drugs.
	Infections—Epstein–Barr virus (EBV), HIV, others.
	Connective tissue disorders—rheumatoid arthritis, systemic lupus erythematosus (SLE), antiphospholipid antibody syndrome.
	Hypersplenism.
	Primary marrow disorder.
Acutely ill patients	Infection/sepsis.
	DIC.
	TTP-HUS.
	Post-transfusion purpura.
Pregnant patient	Gestational (platelet count >70 resolves after pregnancy).
	ITP.
	HELLP—hemolysis, elevated liver enzymes, low platelets.
Cardiac patients	HIT.
	Cardiac bypass.
	Dilutional.
	Gp IIb/IIIa inhibitor-related.
	TTP related to clopidogrel or ticlopidine.
Patient with thrombosis	HIT.
	Antiphospholipid antibody syndrome.
	Paroxysmal nocturnal hemoglobinuria.

- Medication history and review medication chart—particularly, use of heparin, warfarin, and antiplatelet agents including nonsteroidal anti-inflammatory drugs (Table 10.5).
- Heparin-induced thrombocytopenia (HIT) should be considered if the platelet count decreases by 50% and/or thrombosis occurs 5–14 days after starting heparin. 4-T score for pretest probability of HIT is shown in Table 10.6.
- History of known systemic conditions associated with defects in platelets like alcoholism, cirrhosis, HIV infection, systemic lupus erythematosus (SLE), and uremia.
- Family history of excessive bleeding.
- Perform physical examination to look for
  - Evidence of bleeding in skin, mucous membrane, joints, soft tissue
  - Lymphadenopathy
  - Splenomegaly

Table 10.5 Drugs associated with thrombocytopenia

Mechanism	Drugs	
Drug-specific antibody	H_2 receptor blockers	Ranitidine, cimetidine
	Gp IIb/IIIa inhibitors	Abciximab
Drug-dependent antibody	Antibiotics	Vancomycin, rifampicin, chloroquine, amphotericin B, sulfonamides
	Salicylates/NSAIDs	Aspirin, diclofenac, ibuprofen
	Antiepileptics	Valproate, carbamazepine, phenytoin
	Antiarrhythmics	Amiodarone
	Miscellaneous	Quinine, furosemide, thiazide, morphine
Hapten-dependent antibody	Antibiotic	Penicillin, some cephalosporins
Induction of autoantibodies	Antiarrhythmics	Procainamide
	Miscellaneous	Gold salts
Myelosuppression	Antibiotics	Linezolid
	Chemotherapeutic agents	
Unknown	Antibiotics	Fluconazole, daptomycin, ganciclovir, nitrofurantoin, piperacillin
	Miscellaneous	Digoxin, haloperidol
	Gp IIb/IIIa inhibitors	Eptifibatide
Immune complex with PF4	Heparins	Unfractionated and low-molecular-weight heparin
Interference with folate metabolism	Antibiotic	Meropenem
Thrombotic microangiopathy		Clopidogrel, ticlopidine
Pre-existing antibodies		Abciximab

Table 10.6 4-T's score for pretest probability of HIT

Points	2	1	0
Thrombocytopenia (acute)	>50% fall in platelet count	>30% to 50% fall platelet count	<30% fall in platelets
Timing of fall in platelet count	Onset within 5–10 days or,≤ 1 day (if heparin exposure within 30 days)	After day 10, or timing unclear, or ≤ 1 day with recent heparin exposure within 31–100 d	Platelet count fall before day 4 (without recent heparin exposure)
Thrombosis	New thrombosis; skin necrosis or post-heparin bolus acute systemic Reaction	Progressive or recurrent thrombosis; erythematous skin lesions; suspected thrombosis that has not been confirmed	None
Other cause of low platelet	No other cause of platelet count fall is evident	Possible other cause is evident	Definite other cause is present

Pretest probability score: 6–8 high; 4–5 intermediate; 0–3 low

Step 4: Transfuse Platelets (Table 10.7)

- Three types of platelet products are commonly used in clinical practice:
  - Random-donor platelets (RDP)
  - Single-donor platelets (SDP)
  - HLA-matched platelets
- Platelet transfusions are contraindicated in thrombotic thrombocytopenic purpura (TTP), idiopathic thrombocytopenic purpura (ITP), and HIT unless the patient is bleeding.

Step 5: Assess the Rise in Platelet Count after Platelet Transfusion (Table 10.8)

- Platelet counts should be measured 10–60 min after transfusion. Post-transfusion counts at 10–60 min are sensitive to immune platelet destruction. Post-transfusion counts at 24 h assess platelet survival, which is sensitive to nonimmune factors.
- The patient is considered refractory to platelet transfusions if two or three consecutive transfusions are ineffective.
- Alloimmunization is confirmed by demonstrating antibodies to specific human leukocyte antigen (HLA) or human platelet antigen (HPA).

Table 10.7 Platelet transfusion triggers

Transfusion indication	Threshold platelet count (*10^9/L)
Prophylactic transfusion of adult patients	**10**
Before central vein catheter placement	**20**
Urgent diagnostic lumbar puncture	**20**
Before elective diagnostic lumbar punction	**50**
Before major elective surgery (excluding neurosurgery)	**50**
Neurosurgery/eye surgery	100

Table 10.8 Factors associated with platelet refractoriness

Nonimmune factors	Clinical factors	Splenomegaly, fever, infection, bleeding, disseminated intravascular coagulation
	Drugs	Amphotericin B, vancomycin, ciprofloxacin, heparin
	Patient factors	Previous pregnancies, previous transfusions
Immune factors	Antibodies	HLA, platelet specific, erythrocyte
	Others	Length of time the platelets are stored

Step 6: Understand Strategies to Improve Response to Platelet Transfusions (Table 10.9)

- Treat underlying condition.
- Transfuse ABO identical platelets.
- Transfuse platelets less than 48 h in storage.
- Increase the number of platelets transfused.
- Select compatible donor: HLA-matched, ABO compatible.

Table 10.9 Approach for the management of thrombocytopenia

Etiology	Mechanism	Presentation	Treatment
ITP, after viral illness, may be associated with antiphospholipid antibody syndrome, may be initial presentation of connective tissue disease, lymphoproliferative malignancy	IgG antibodies against platelet antigens, platelet clearance by spleen, inadequate platelet production response	All ages, common in young adult females	Steroids, prednisolone 1 mg/kg/day for 1–2 weeks, taper
		Severe thrombocytopenia with normal RBC and WBC morphology and number	IVIG infusion 1 g/kg/day for 2 days
		Diagnosis by exclusion	Anti RhD antibodies 50–75 μ/kg IV (Rh + Ve patients with intact spleen)
TTP-HUS	Inherited or acquired deficiency of von Willebrand factor cleaving protease (ADAMTS13)	Microangiopathic hemolytic anemia, thrombocytopenia, renal insufficiency, fever, and mental status changes	FFP transfusions until the patient is ready for plasma exchanges
	Idiopathic or secondary to *Escherichia coli* diarrhea, HIV infection, certain drugs (ticlopidine, clopidogrel, quinine, cyclosporine A, mitomycin A, cisplatin, etc.), pregnancy, bone marrow transplant, and metastatic carcinomas	Schistocytes in peripheral smear, raised LDH, normal coagulation profile	Plasma exchanges
			Platelet transfusions only in life-threatening bleeding

(continued)

Table 10.9 (continued)

Etiology	Mechanism	Presentation	Treatment
Drug-induced thrombocytopenia	Antiplatelet agents' and other drugs' immune mechanism	History—no other blood or coagulation abnormalities	Stop the offending drug
			Supportive care
	Chemotherapy and alcohol—directly inhibit megakaryocytes	Most chemotherapeutic drugs—the nadir of blood counts in 7–10 days, recover over 2–3 weeks nitrosureas and mitomycin cause prolonged myelosuppression	Supportive care
	Heparin—antibodies against heparin–platelet factor 4 complex	Type I—modest transient thrombocytopenia in 2–3 days after heparin therapy	Spontaneous recovery
		Type II—less common, occurs 4–14 days after heparin therapy	Stop heparin
		ELISA assay for anti-PF 4 antibody, serotonin release assay, platelet aggregation studies	Doppler to rule out thrombosis
			Use direct thrombin inhibitors (argatroban, lepirudin) Fondaparinux should be used with caution
			LMWH and UFH should not be used

Step 7: Treat the Underlying Cause

- Review and stop all offending medication.
- Evaluate the patient for evidence of secondary infection or DIC.

Step 8: Role of Thrombopoiesis-Stimulating Agents (Table 10.10)

Thrombopoiesis-stimulating agents can be used to promote platelet production. Thrombopoiesis is a dynamic process of the development of platelets mainly taking place in bone marrow and lungs This process is regulated by various signaling pathways and thrombopoietin (THPO) is a primary regulatory cytokine.

There are various drugs that have shown promising results in clinical settings.

Table 10.10 Thrombopoiesis-stimulating agents

Drug name	Mechanism of action	Indication
Pegylated recombinant human megakaryocyte growth and development factor (PEG-rHuMGDF)	Activates THPO-MPL signaling.	Chemotherapy-induced thrombocytopenia
Recombinant human thrombopoietin (rHuTHPO)	Activates THPO-MPL signaling.	Chemotherapy-induced thrombocytopenia
Romiplostim	Thrombopoietin receptor agonists. Activates THPO-MPL signaling.	Immune thrombocytopenia (ITP), chemotherapy-induced thrombocytopenia, post-bone marrow transplant thrombocytopenia, thrombocytopenia related to chronic liver disease, aplastic anemia
Eltrombopag	Thrombopoietin receptor agonists. Activates THPO-MPL signaling.	ITP, post-bone marrow transplant thrombocytopenia, aplastic anemia
Avatrombopag	Thrombopoietin receptor agonists. Activates THPO-MPL signaling.	ITP, thrombocytopenia related to chronic liver disease
Lusutrombopag	Thrombopoietin receptor agonists. Activates THPO-MPL signaling.	Thrombocytopenia related to chronic liver disease
Hetrombopag	Thrombopoietin receptor agonists. Activates THPO-MPL signaling.	ITP

Suggested Reading

Alessandro Squizzato UOC. Medicina I: Supportive management strategies for disseminated intravascular coagulation. An international consensus. Thromb Haemost. 2016;115(5):896–904. *A review article that provides evidence and expert-based recommendations on the optimal supportive hemostatic and antithrombotic treatment strategies for patients with DIC based on five relevant clinical scenarios explained by international experts*

Levi M, Toh CH, Thachil J, Watson HG. Guidelines for the diagnosis and management of disseminated intravascular coagulation. Br J Haematol. 2009;145:24–33. *Are evidence-based guidelines, diagnosis, and management of DIC*

Levi M. Current understanding of disseminated intravascular coagulation. Br J Haematol. 2008;124:567–76. *A very good review on pathogenesis of DIC*

Napolitano LM, Warkentin TE. Heparin-induced thrombocytopenia in the critical care setting: diagnosis and management. Crit Care Med. 2006;34(12):2898–911. *This review article summarizes the pathogenesis and clinical consequences of HIT, describes the diagnostic process, and reviews currently available treatment options*

Rice TW, Wheeler AP. Coagulopathy in critically ill patients: part 1: platelet disorders. Chest. 2009;136(6):1622–30. *This article reviews the most frequent causes of thrombocytopenia by providing an overview of the following most common mechanisms: impaired production, sequestration, dilution, and destruction. Guidelines for treating thrombocytopenia and platelet dysfunction are also provided*

Thachil J. Disseminated intravascular coagulation a practical approach. Anesthesiology. 2016;125:230–6. *A practitionar guide for the management of DIC*

Thachil J, Warkentin TE. How do we approach thrombocytopenia in critically ill patients? Br J Haematol. 2017;177:27–38. *A review of an approach to thrombocytopenia*

Toh CH, Alhamdi Y, Abrams ST. Current pathological and laboratory considerations in the diagnosis of disseminated intravascular oagulation. Ann Lab Med. 2016;36(6):505–12. *This is a concise review article that provides a practical diagnostic tool for acute DIC, a composite scoring system using rapidly available coagulation tests. Its usefulness and limitations are discussed alongside the advances and unanswered questions in DIC pathogenesis*

Vincent JL, Francois B, Zabolotskikh I. Effect of a recombinant human soluble thrombomodulin on mortality in patients with sepsis-associated coagulopathy: the SCARLET Randomized Clinical Trial. JAMA. 2019; *Randomized controlled trial of patients with sepsis-associated coagulopathy were randomized and treated with an intravenous bolus or a 15-minute infusion of thrombomodulin (0.06 mg/kg/d [maximum, 6 mg/d]; n = 395) or matching placebo (n = 405) once daily for 6 days. The primary end point was 28-day all-cause mortality. 28-day all-cause mortality rate was not statistically significantly different between the thrombomodulin group and the placebo group.The incidence of major bleed was somewhat higher in the thrombomodulin group*

Website

http://www.bcshguidelines

11

TTP/HUS and HLH Syndromes

Gunjan Chanchalani, Seema Tekwani, and Vivek Dave

Thrombotic Thrombocytopenic Purpura (TTP)/Hemolytic Uremic Syndrome (HUS)

A 36-year-old female homemaker was brought to the emergency room (ER) with a 7-day history of moderate-grade fever without chills. She had experienced altered sensorium for 3 days and one episode of jerky body movements 3 days ago. Her family reported that she had been feeling fatigued and lethargic, along with passing dark-colored urine for the past 2 weeks.

On examination, she was drowsy and sluggish in her responses, with no obvious focal neurological deficits. Her Glasgow coma scale (GCS) was 11/15 (E3M5V3). She appeared pale, with evidence of mild icterus and a peripheral purpuric rash. She was febrile, with a pulse of 116/min, regular, blood pressure of 130/70 mmHg, a respiratory rate of 28/min, and oxygen saturation of 97% on room air. She also had a history of diabetes for the past 2 years and had been taking herbal medicine for the last 2 years.

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Thrombotic thrombocytopenic purpura (TTP) and hemophagocytic lymphohistiocytosis (HLH) are both rare hematological conditions, occurring due to pathological immune dysregulation, and are associated with high mortality. They both occur due to overlapping trigger factors; however, they do not coexist usually. The diagnosis is often challenging and delayed due to the rarity of the disease, thus worsening the prognosis.

Step 1: Resuscitate

- Do initial resuscitation as described in Chap. 24.
- Airway—Often patients present with low sensorium and seizures, and it is important to assess the airway and the need for protection.

Step 2: Take Focused History and Do the Examination

- Fever, fatigue, and malaise are often seen in patients.
- Jaundice may be seen due to hemolysis, leading to unconjugated hyperbilirubinemia.
- Bleeding episodes in the form of petechiae, epistaxis, gum bleeding, hematuria, glycemic index (GI) bleeding, etc., are often seen due to thrombocytopenia.
- Neurological signs and symptoms include headaches, seizures, slurred speech, confusion, encephalopathy, and even coma.
- Cardiac involvement presents as chest pain, heart failure, or is seen as raised serum troponin levels and is a poor prognostic sign.
- Acute renal failure needing dialysis is often seen in HUS but is a rare occurrence in TTP.
- Ischemic complications may be seen affecting any organ, including the GI tract.
- Look for a history of acute blood loss.
- History of diarrhea due to *Shigella* or *E. coli* O157:H7 raises suspicion of classic HUS.

Step 3: Make a Differential Diagnosis

- Meningoencephalitis (bacterial/viral)
- Metabolic encephalopathy
- Tropical infections—cerebral malaria, scrub typhus
- Sepsis
- Hemolysis—infection-induced/autoimmune/blood transfusion-related
- Disseminated intravascular coagulation (DIC)

Step 4: Order Investigations

- Complete blood count.
  - Hb is low
  - Platelets often less than 30 × 10^9/L
- Reticulocyte count is increased with low haptoglobin levels.
- Blood smear examination—Presence of schistocytes/fragmented Red Blood Cells (RBCs). Schistocytes are fragmented RBCs from intravascular hemolysis (>0.5% suggests the presence of microangiopathic hemolytic anemia).
- Coagulation profile is normal.
- Liver enzymes are normal, with unconjugated hyperbilirubinemia.
- Renal function may be impaired:
  - TTP causes AKI in <50% of patients and is usually mild.
  - HUS causes severe AKI.
- Urine analysis—evidence of proteinuria, macrohematuria.
- Cardiac involvement is seen as raised troponin levels.
- Lactate dehydrogenase levels are raised due to hemolysis and tissue ischemia.
- Send aerobic culture sensitivity to rule out infection and sepsis.
- Send blood for blood group and cross-matching.
- Do CT brain to rule out intracranial pathology. However, absence of focal neurological deficit grossly rules out any intracranial lesion.
- Stool PCR—Shiga toxin genes, stool culture, and/or bioassay of stool for Shiga toxin.

Step 5: Suspect and Make a Diagnosis of TTP /HUS

- The diagnosis should be suspected based on clinical history and laboratory findings.
- Thrombotic microangiopathy (TMA) has three hallmark features:
  - (i) Thrombocytopenia (<150 × 10^9/L, or >25% drop from baseline)
  - (ii) Microangiopathic hemolytic anemia (MAHA)—anemia, schistocytes, raised LDH, low haptoglobin, indirect bilirubin elevated
  - (iii) Associated organ damage due to microvascular/macrovascular occlusion which frequently involves the kidney, brain, GI tract, and heart

$$\text{TMA} = \text{Thrombocytopenia} + \text{MAHA} + \text{End} - \text{organ Damage}$$

- The diagnostic criteria for HUS and TTP are shown in Table 11.1.
- PLASMIC score
  - Helps determine the likelihood of TTP.
  - One point is assigned for each criterion, and the score ranges from 0 to 7 (Table 11.2).
  - Score 0–4 suggests that TTP is unlikely (0–4% likelihood).
  - Score 5–7 (score of 6–7 suggests 62–82% likelihood of TTP) has a high sensitivity for TTP and suggests a benefit from plasmapheresis unless there is a possible alternative diagnosis.

Table 11.1 Diagnostic clinical features of HUS and TTP

Diagnostic triad of HUS
MAHA
Thrombocytopenia
Acute kidney injury
Diagnostic pentad of TTP
MAHA—e/o schistocytes in peripheral blood smear
Thrombocytopenia
Renal failure
Fever
Altered mental status

Table 11.2 Criteria for PLASMIC score

Platelet count (30 × 10^9/L)
Hemolysis—Reticulocyte reticulocyte >2.5%, undetectable haptoglobin, indirect bilirubin >2 mg/dL
No active malignancy within 1 year
No history of transplantation
MCV < 90 fL
INR < 1.5
Serum Creatinine <2 mg/dL (with normal baseline

Table 11.3 Differential diagnosis of thrombotic microangiopathy

Disseminated intravascular coagulation DIC
Pregnancy associated—HELLP/eclampsia
Autoimmune (vasculitis, lupus nephritis acute scleroderma)
Malignant hyperthermia
Catastrophic antiphospholipid syndrome
Severe bacterial infection (meningococcus, pneumococcus)

Step 6: Confirm the Diagnosis

1. ADAMTS13 activity (normal >60%).
   - ADAMTS13 assays help confirm the diagnosis.
   - Patients with TTP have plasma ADAMTS13 activity less than 10% of normal or <10 IU/dL.
   - In HUS, it is more than 10% of normal ADAMST13 activity.
   - The diagnosis of HUS should be considered only after other secondary causes of thrombotic microangiopathy have been excluded (Table 11.3).
2. ADAMTS13 inhibitor
   - Acquired TTP has antibodies that block the activity of ADAMTS13.
   - These cases have normal ADAMTS13 activity.
   - Detected by mixing studies.
   - ELISA assays have increased sensitivity to detect antibodies against ADAMTS13.

Table 11.4 Trigger factors for HUS/TTP

1. Malignancy, especially hematological malignancy (lymphoma, acute lymphoblastic leukemia), bone marrow transplantation
2. Infections
Viral—Cytomegaloviruscytomegalovirus, Ebstein–Barr virus, human immunodeficiency virus
Bacterial
Fungal
3. Autoimmune disorders—Lupus
4. Pregnancy
5. Drugs—e.g.: Calcineurin inhibitors, Ticlopidine

Step 7: Look for a History of Triggering Factors

- Look for triggering factors—both the conditions have overlapping triggering factors (Table 11.4).

Step 8: Do Specific Management

1. Fresh-frozen plasma (FFP) transfusion
    - FFP contains ADAMTS13 and should be considered if plasmapheresis will be delayed for more than 6–8 h.
2. Plasmapheresis/plasma exchange
    - Therapeutic plasma exchange is the mainstay of treatment for TTP.
    - It removes ADAMTS13 neutralizing autoantibodies and other harmful cytokines from the plasma and helps replenish ADAMTS13 activity.
    - Plasma exchange should be initiated promptly, pending the results of ADAMTS13 levels, preferably within 4 h of a suspicion, to reduce mortality.
    - Insert hemodialysis catheter under USG guidance by an expert operator.
    - Dose: 1.5 times plasma volume exchange/60 mL per kg.
    - Daily plasmapheresis should be continued till platelet count is normal ($>150 \times 10^9$/L) for two consecutive days.
    - In patients with life-threatening complications, plasmapheresis may be performed twice daily.
    - Daily plasmapheresis has been shown to reduce mortality to 10–20%.
    - Correct hypocalcemia.
    - Monitor LDH.
3. Do not give platelets. Platelet transfusion should be avoided as it is associated with an increase in mortality.
4. Corticosteroids.
    - High-dose methylprednisolone of 10 mg/kg/day should be given for 3 days followed by 2.5 mg/kg/day.
    - They should be tapered after platelet counts normalize.

5. Rituximab.
   - Rituximab when used in acute stages has been shown to reduce the number of plasmapheresis days, relapse, and mortality.
   - Rituximab is also useful in refractory TTP or in cases of relapse.
   - When used along with plasmapheresis, rituximab should be administered every 3–4 days.
6. Caplacizuamb.
   - First dose to be administered as IV.
   - Later given subcutaneously once daily for up to 30 days after the completion of plasmapheresis.
   - Its use has been shown to reduce the length of ICU stay, the need for plasmapheresis, duration of thrombocytopenia, occurrence of relapse, and refractory cases.
7. Additional immunosuppressive therapy.
   - Cyclosporin, mycophenolate mofetil, azathioprine, cyclophosphamide, daratumumab, and bortezomib may be used.
   - Severe and recurrence may need a splenectomy.
8. Anticomplement C5 monoclonal antibodies—eculizumab or rovelizumab are life-saving treatment options for complement-mediated HUS.
9. Prophylactic antibiotics should be administered against encapsulated bacteria throughout therapy.
10. Avoid blood transfusion.
    - Target Hb 7 mg/dL.
11. DVT prophylaxis should be started when platelet count >30 × 10^9/L.
12. Treatment of Shiga toxin HUS is supportive.
13. Complement-mediated HUS requires urgent treatment with eculizumab.

Step 9: Prognosticate

- TTP is life-threatening.
- Almost complete neurological recovery is seen with aggressive therapy.
- ADAMTS13 assay levels help monitor the course of the disease and further need for any additional treatment.
- Poor prognostic markers include age >60 years, Caucasian ethnicity, evidence of arterial thrombosis, coma, and raised troponin levels.

Hemophagocytic Lymphohistiocytosis (HLH)

A 27-year-old male corporate worker presented with a high-grade fever lasting over a month, accompanied by vomiting and a 10 kg weight loss since the onset of the illness. He has no comorbidities or history of tuberculosis exposure. On examination, he is drowsy and obtunded with no focal neurological deficits. His vital signs reveal a temperature of 38.7 °C, pulse of 118/min, and blood pressure of 108/78 mmHg. Cervical lymphadenopathy is noted, but there is no skin rash. Systemic examination is grossly normal.

Step 1: Resuscitate

- Do initial resuscitation as described in Chap. 24.
- Protect the airway if the patient has low GCS and maintain oxygen saturation of 94%.
- Circulation—do fluid resuscitation to maintain MAP >65 mmHg.

Step 2: Take Focused History and Examination

- The patient has a varying presentation, and hence, the diagnosis is often missed.
- Nonspecific symptoms of fever, malaise, and fatigue are often seen.
- Fever is common and may be high-grade.
- Splenomegaly is one of the common findings.
- Hepatomegaly, rashes, diffuse lymph node enlargement, and jaundice may be present.
- Neurological manifestations in the form of seizures, retinal hemorrhages, ataxia, and altered consciousness can also be present.
- Patients may progress to multiorgan dysfunction syndrome (shock, acute renal failure, acute liver failure, acute respiratory distress syndrome).
- The disease has overlapping findings with sepsis and multiorgan failure.
- CNS dysfunction and bacterial and fungal infections due to prolonged neutropenia can also occur.
- In the case of genetic HLH, atypical symptoms in the form of chronic diarrhea and sensorineural hearing loss are seen. The clinical condition resembles chronic variable immune deficiency.

Step 3: Make a Differential Diagnosis

The diagnosis is often missed due to its varying presentation and lack of awareness.

1. Sepsis
2. Tuberculosis, infectious mononucleosis
3. DRESS (drug reaction with eosinophilia and systemic symptoms)
4. Fulminant hepatic failure in pediatrics
5. Viral encephalitis or CNS vasculopathy
6. Langerhans cells histiocytosis

Step 4: Send Investigations

- Complete blood count
  - Usually bi-cytopenia >75% of patients
- Peripheral smear—leucopenia, mild neutropenia, with low platelets.
- CRP is raised.
- Procalcitonin may be negative.
- Ferritin—highly raised, >2000 microg/L—ferritin has a good negative predictive value.
- LDH—high.
- Hyperfibrinolysis—low fibrinogen levels, increased D dimer.
- Triglyceride level (fasting)—elevated.
- Liver transaminases—raised, hyperbilirubinemia.
- Kidney functions are often normal, unless multiorgan involvement.
- Send cultures and sensitivity—two sets of blood cultures, urine culture.
- Routine workup for tropical illness—usually shows no growth.
- Tropical panel and blood PCR for herpes viruses (especially Epstein-barr virus (EBV), cytomegalovirus (CMV), and Herpes simplex virus (HSV)) to be ruled out.
- CT chest—to look for lymphadenopathy.
- USG—to look for hepatosplenomegaly.
- Lumbar puncture and/or MRI if suspicion of brain involvement.
- Biopsy/FNA of involved sites (especially bone marrow or lymph nodes). The typical microscopic findings include hemophagocytosis seen in lymphocytes and macrophages. Bone marrow is the most common site but can also be seen in lungs, cerebrospinal fluid (CSF), meninges, liver, spleen, lymph nodes, and even in subcutaneous sites. However, the presence of hemophagocytosis is not specific to the diagnosis of HLH in the absence of other features.
- Soluble IL-2 receptor (a.k.a. soluble CD25)—increased in HLH. Poor sensitivity and specificity.

Step 5: Assess the Possibility of HLH

- A biopsy-proven histopathology is not mandatory for the diagnosis of HLH.
- Two scoring systems are widely used for the diagnosis of HLH.
  - HLH2004 criteria/Henter 2004 criteria (Table 11.5). Mainly for pediatric formulation.
  - Not validated for use in adults or cases of secondary HLH.
- *Hscore*
  - An online calculator (www.mdcalc.com)
  - More appropriate for use in adults
  - Takes into consideration immunosuppression, fever, organomegaly, hypertriglyceridemia, ferritin, aspartate aminotransferase (AST)/ serum glutamic oxaloacetic transaminase (SGOT), fibrinogen, cytopenias of only one or more cell lineages, and hemophagocytosis in bone marrow samples.
  - The total score varies from 0 to 337, and the optimal cut-off for diagnosis is 169, which has a sensitivity of 93% and a specificity of 86%.
  - The sensitivity and specificity of the Hscore are greater in the pediatric group (100% and 80%, respectively) than in adults (90% and 79%, respectively).
  - However, there is not much difference between the sensitivity and specificity for HLH2004 and Hscore in critically ill adult patients.

Table 11.5 HLH2004 criteria

Four of the eight criteria listed below should be present:
1. Fever ≥38.3 °C
2. Splenomegaly
3. Cytopenia (involving at least two of the three lineages in the peripheral blood)
Hemoglobin <9 g/dL (infants up to 4 weeks: hemoglobin <10 g/dL)
Platelets <1,00,000/μL
Neutrophils <1000/μL
4. Hypertriglyceridemia (≥265 mg/dL) and/or hypofibrinogenemia (≤150 mg/dL)
5. Hemophagocytosis in the bone marrow or spleen or lymph nodes or liver
6. Low or absent NK cell activity
7. Ferritin ≥500 ng/mL
8. sCD25 (soluble form of CD25) (sIL2-Ra) ≥2400 U/mL

Step 6: Look for Precipitating Factors

There are many triggers for the disease:

- Infections
  - Viral—EBV most common, other CMV, HSV, VZV
  - Bacterial—*Bartonella*, tuberculosis, *Legionella*
  - Fungal—histoplasma
  - Parasites—*Leishmania*, *Plasmodium*
  - HIV
- Rheumatic conditions—SLE, juvenile rheumatoid arthritis
- Post-transplant
- Malignant diseases—hematological in 90% of cases
- Drug hypersensitivity
- Familial HLH

Step 7: Treat the Underlying Cause

- Identify and aggressively treat the underlying cause of the HLH.
- Malignancy: combination chemotherapy may be needed.
- Infection: appropriate antimicrobial therapy. Rituximab may reduce viral load and improve EBV-associated HLH.
- Rheumatologic disease flare: management may require pulse-dose steroid or augmented immunosuppressive regimens.

Step 8: Start Immunosuppression

- Dexamethasone:
  - 10 mg/m^2 body surface area (~15–20 mg/day) at least.
  - 40 mg/day for patients not receiving other immunosuppressive therapy.
  - HLH with macrophage activation syndrome or neurological involvement—consider pulse steroid 1000 mg/.
  - Rule out infection.
  - Secondary HLH: consider 10 mg/m^2/day dexamethasone plus one of the following:
- Anakinra (especially infection or rheumatologic related).
  - Second-line agent for HLH
  - For immunomodulation
  - Without immunosuppression
- Ruxolitinib (especially in malignancy or EBV related)
- Cyclosporine—robust evidence is lacking

- Etoposide
  - Most appropriate for patients with familial HLH.
  - Severe EBV-related HLH.
  - Neurological manifestations:
  - HLH that is refractory to other therapies.
- Familial HLH: consider moderate-dose dexamethasone plus etoposide.
- Salvage therapy for relapsed and refractory cases
- The following agents can be used
  - Cyclophosphamide, doxorubicin, vincristine, prednisone (CHOP)-like regimens
  - With etoposide
  - Anti-CD52 antibody alemtuzumab
  - Cytokine adsorption cartridges or plasmapheresis
  - Ruxolitinib JAK2 inhibitor (off-label)
  - Emapalumab anti-IFN-γ antibody
- Macrophage activation syndrome treatment
- Treated with high-dose corticosteroids.
- Does not require cytotoxic treatment.
- Cyclosporine A may be used in patients not responding to steroids.
  - HLH2004 may be considered for patients not responding to steroids and cyclosporine A.
  - Other alternatives with less efficacy and more side effects include anti-thymocyte globulin, plasmapheresis, intravenous immunoglobulin (IVIG) and cyclophosphamide, biological agents like Anakinra, and an IL-1 receptor antagonist have also been tried recently.

Step 9: Protocols for Treatment

1. HLH94 protocol
   - Widely used.
   - 8-week therapeutic dose of etoposide (150 mg/m^2 twice weekly for 2 weeks and then weekly) plus dexamethasone (initial dose of 10 mg/m^2 slowly tapered over 8 weeks).
   - Those patients who have familial disease or persistent disease should be continued on above treatment till allogenic stem cell transplant has been done.
   - Pulses of dexamethasone (10 mg/m^2 for 3 days every second week) and etoposide (150 mg/m^2 every alternating second week) with daily oral cyclosporine therapy should be given as continuation treatment.
   - Those with neurological findings benefit from intrathecal methotrexate.
   - Adult treatment is almost the same as pediatric population, but since adults have more comorbidities, the chances of end-organ damage due to cytokine surge are very high.

2. HLH2004 protocol
   - Similar to the HLH94 protocol
   - Only difference is that starting of cyclosporine A in the initiation phase itself at the beginning so as to get immunosuppression and oppose the action of IFN-γ.
   - Hemopoietic stem cell transplant is performed as soon as the donor is available.
   - It is advisable to administer intrathecal prednisolone along with methotrexate for patients with neurological symptoms.

Step 10: Hematopoietic Stem Cell Transplantation

- Cure for familial HLH in patients who have a risk of hematological malignancy.
- If donors do not match, then unrelated mismatched donors may be used as the disease is fatal.
- The bone marrow undergoes myeloablative conditioning using busulfan, cyclophosphamide, etoposide with or without antithymocyte globulin, or reduced-intensity conditioning using melphalan/treosulfan, fludarabine, and alemtuzumab with or without antithymocyte globulin.
- Unrelated umbilical cord blood is also tried.

Step 11: Monitor Parameters to Track Response to Therapy

- Fever curve.
- Ferritin level: higher values and failure to reduce is associated with worse outcomes. In untreated HLH, serum ferritin keeps increasing rapidly.
- C-reactive protein.
- D-dimer and fibrinogen levels.
- Liver function tests.
- Cytopenias (complete blood count).

Prognosis varies and is often fatal in untreated cases. Prognosis is worse in patients with underlying hematological malignancy, age >50 years, high ferritin, slow decline in ferritin levels with treatment, neurological involvement, and associated DIC.

Suggested Reading

Al-Samkari H, Berliner N. Hemophagocytic lymphohistiocytosis. Annu Rev Pathol. 2018;13:27–49. https://doi.org/10.1146/annurev-pathol-020117-043625. Epub 2017 Sep 13

Arnold DM, Patriquin CJ, Nazy I. Thrombotic microangiopathies: a general approach to diagnosis and management. CMAJ. 2017;189(4):E153–9. https://doi.org/10.1503/cmaj.160142.

Brisse E, Matthys P, Wouters CH. Understanding the spectrum of haemophagocytic lymphohistiocytosis: update on diagnostic challenges and therapeutic options. Br J Haematol. 2016;174:175–87.

Donadelli R, Sinha A, Bagga A, Noris M, Remuzzi G. HUS and TTP: traversing the disease and the age spectrum. Semin Nephrol. 2023;43(4):151436. https://doi.org/10.1016/j.semnephrol.2023.151436.

Matsumoto M, Miyakawa Y, Kokame K, et al. Diagnostic and treatment guidelines for thrombotic thrombocytopenic purpura (TTP) in Japan 2023. Int J Hematol. 2023;118:529–46. https://doi.org/10.1007/s12185-023-03657-0.

Michael M, Bagga A, Sartain SE, Smith RJH. Haemolytic uraemic syndrome. Lancet. 2022;400(10364):1722–40. https://doi.org/10.1016/S0140-6736(22)01202-8.

Schram AM, Comstock P, Campo M, Gorovets D, Mullally A, Bodio K, Arnason J, Berliner N. Haemophagocytic lymphohistiocytosis in adults: a multicentre case series over 7 years. Br J Haematol. 2016;172(3):412–9. https://doi.org/10.1111/bjh.13837. Epub 2015 Nov 5

Scully M, Rayment R, Clark A, et al. A British Society for Haematology Guideline: diagnosis and management of thrombotic thrombocytopenic purpura and thrombotic microangiopathies. Br J Haematol. 2023;203(4):546–63. https://doi.org/10.1111/bjh.19026.

Thompson GL, Kavanagh D. Diagnosis and treatment of thrombotic microangiopathy. Int J Lab Hematol. 2022;44(Suppl 1):101–13. https://doi.org/10.1111/ijlh.13954.

Onco-emergencies

12

Atul Kulkarni and Vandana Agarwal

Hypercalcemia

A 58-year-old male patient with metastatic renal cell carcinoma presented with lethargy, confusion, anorexia, nausea, and constipation. He was polyuric and polydipsic over the past few days. He was found to be hypercalcemic. Hypercalcemia is mostly seen in solid tumors such as squamous cell carcinoma of the head, neck, and lungs, breast cancer, ovarian cancer, renal carcinoma, and some hematological malignancies, for example, leukemia, lymphoma, and multiple myeloma. A high index of suspicion is needed in patients with malignancy.

Oncological emergencies such as hypercalcemia, tumor lysis syndrome, superior vena cava syndrome, and spinal cord compression are occasionally seen as an intercurrent problem or presenting manifestations in certain cancers.

Step 1: Resuscitate

Hydration is paramount in these patients, and intravenous saline should be given rapidly once hypercalcemia is confirmed.

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Step 2: Send Investigations

- Measure ionized serum calcium (arterial or venous).
- Mild hypercalcemia (<12 mg/dL or 3 mmol/L) does not require immediate treatment. Moderate-to-severe hypercalcemia (14 mg/dL or 3.5 mmol/L) is usually symptomatic and requires treatment.
- A low serum chloride level (<100 mEq/L) suggests hypercalcemia of malignancy.
- If total serum calcium is measured, correct the albumin level. Corrected calcium = measured total calcium + [0.8 × (4.0-albumin)].
- Also, check serum creatinine, electrolytes including phosphates, and alkaline phosphatase. Phosphorus should be monitored and repleted as hypophosphatemia is associated with hypercalcemia,
- ECG abnormalities reflect altered transmembrane potentials, affecting conduction such as QT interval shortening (common) and QRS interval lengthening (high levels). T waves may flatten, or invert and a variable degree of heart block may develop (Fig. 12.1).

The above ECG shows a short QT interval with hardly any ST segment, characteristic of hypercalcemia. In this tracing, the QRS complexes are wide, indicative of an intraventricular conduction defect. No P waves are evident, and this is most likely a junctional escape rhythm.

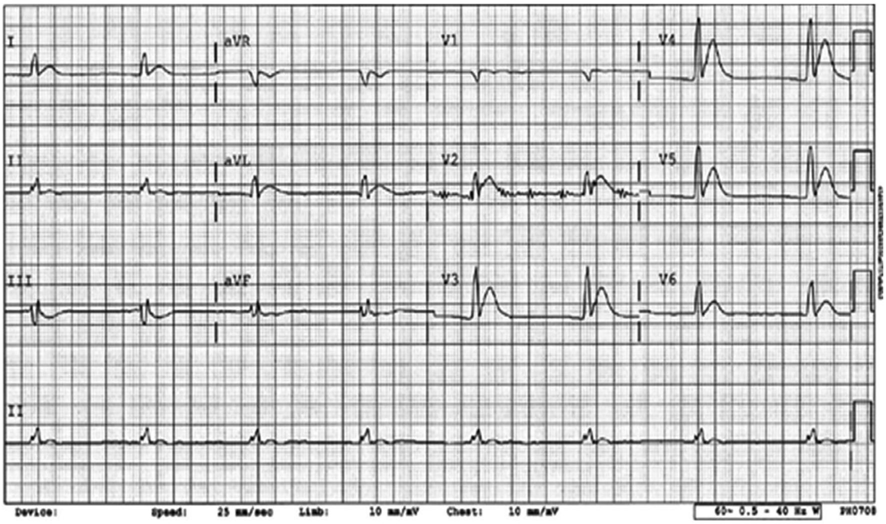

Fig. 12.1 ECG changes in hypercalcemia

Step 3: Infuse Fluid

- Severe hypercalcemia is usually associated with marked hypovolemia.
- Give 500–1000 mL of normal saline in the first hour and continue at 200–300 mL/h until restoration of intravascular volume and urine output of more than 100 mL/h is established. Intravenous hydration helps in increasing urinary calcium excretion.
- In patients with impaired cardiorespiratory and renal function, fluid resuscitation should be done cautiously with close hemodynamic monitoring.

Step 4: Start Diuretics after Fluid Repletion

- Diuretics promote urinary calcium excretion by inhibiting calcium reabsorption.
- Consider loop diuretics only when euvolemia is achieved as hypovolemia causes renal hypoperfusion hampering calcium excretion. They are specifically useful if features of hypervolemia, secondary to aggressive fluid resuscitation, develop, and in cases of associated cardiac and renal impairment.

Step 5: Start Specific Therapy (Table 12.1)

- Bisphosphonates block osteoclastic bone resorption. Its action is evident in 2–3 days and lasts for 2–4 weeks. It is preferred in hypercalcemia secondary to malignancy as it is more potent and can be given over a shorter course of time. However, it can cause osteonecrosis of the jaw and nephrotoxicity in long-term use.

Table 12.1 Treatment for hypercalcemia

Intervention	Dosage	Comment
Normal saline	250–500 mL/h until euvolemic, thereafter 200–300 mL/h IV, may require 3–4 L Keep urine output 100–150 mL/h	Caution in patients with congestive heart failure
Furosemide	20–40 mg IV	After restoration of intravascular volume
Bisphosphonates	Pamidronate: 60–90 mg IV 2–4 h Zoledronic acid: 4 mg IV over 15 min	Caution in renal impairment
Calcitonin	4–8 IU/Kg SC or IV every 12 h	Rapid onset, but short-lived
Glucocorticoids	Prednisolone: 60 mg/day PO Hydrocortisone: 100 mg IV every 6 h	Hyperglycemia, immunosuppression
Denosumab	120 mg SC every 4 weeks Give two additional 120 mg doses during the first month of therapy on days 8 and 15	Rule out chronic kidney disease-related mineral bone disorder

- IV bisphosphonate of choice is zoledronic acid, 4 mg IV over 15 min. Use zoledronic acid with caution in patients with renal impairment and adjust the dose according to creatinine clearance (Table 12.1).
- Calcitonin (subcutaneous or intramuscular) 4 units/kg lowers calcium levels quickly (acts within 4–6 h and lasts for about 2 days), but the effect is short-lived. It prevents bone resorption and increases urinary calcium excretion.
- In some patients with lymphomas, particularly Hodgkin's disease, hypercalcemia is caused by elevated levels of vitamin D ($1,25(OH)_2D$); glucocorticoids are particularly effective as they decrease vitamin D production and calcium absorption from the intestines.
- Denosumab acts by inhibiting receptor activators of nuclear factor kappa beta (RANKL). It should be considered when there is no response to zoledronic acid or in patients with kidney impairment as this drug is not cleared by the kidneys. There is a higher risk of hypocalcemia with denosumab in patients with renal impairment.

Step 6: Decrease Intake

- Eliminate dietary sources of calcium.

Discontinue medications such as thiazide diuretics (increase the reabsorption of calcium) and vitamin D that increase the calcium level.

Step 7: Consider Dialysis

- Dialysis should be considered for patients with renal failure and/or congestive heart failure when aggressive hydration and bisphosphonates cannot be used safely.
- Calcimimetic agents, such as cinacalcet, are preferred in hemodialysis patients and hypercalcemia secondary to parathyroid cancer.

Step 8: Treat the Cause

- Treat the malignancy with chemotherapy and radiation to control the hypercalcemia if feasible.

Step 9: Evaluate the Prognosis

- In patients with advanced malignancy, hypercalcemia may commonly occur.
- In such circumstances, it may be appropriate, ethical, and humane to institute only comfort measures if no effective treatment for malignancy exists.

Tumor Lysis Syndrome

- *A 26-year-old patient, with Burkitt's lymphoma recently started on chemotherapy, presented with anorexia, lethargy, disorientation, dyspnea, tachypnea, vomiting, muscle cramps, and decreased urine output.*
- Tumor lysis syndrome is most seen in solid tumors. Tumor lysis also occurs in hemato-oncological malignancies, for example, acute lymphoblastic leukemia, high-grade lymphomas with a high tumor burden. It can occur spontaneously or after initiation of chemotherapy, radiotherapy, or even corticosteroid therapy. Excessive lysis of tumor cells leads to the release of intracellular chemical substances, which in turn causes hyperkalemia, hyperuricemia, hyperphosphatemia, and hypocalcemia. It is a medical emergency and can lead to end-organ damage. Deposition of uric acid and/or calcium phosphate crystals in renal tubules can result in acute kidney injury.

Step 1: Resuscitate

- These patients are usually dehydrated and will benefit from intravenous fluids (refer Chap. 24). Rapid volume expansion will help increase the glomerular filtration rate, which helps in the excretion of solutes.

Step 2: Make a Diagnosis

- Investigations may show hyperuricemia, hyperkalemia, hyperphosphatemia, hypocalcemia, uremia, and raised lactate dehydrogenase levels.
- Obtain an electrocardiogram to rule out serious arrhythmias due to hyperkalemia and conduction abnormalities.
- Check urine output and renal function.

Step 3: Start Hydration

- A high infusion rate of fluids is appropriate.
- Patients with a high risk of tumor lysis syndrome should have aggressive volume replacement as a preventive measure prior to chemotherapy.
- Infuse isotonic fluid at a rate of 200–300 mL/h.
- Volume should be adapted for the patient's age, cardiac and renal function, and urine output.
- Increasing the urinary flow rate is the most effective strategy for preventing urate-induced obstructive uropathy.
- Urine output should be maintained within a range of 80–100 mL/m^2/h.
- Urine-specific gravity should be maintained at ≤ 1.010 (Table 12.2).

Table 12.2 Treatment for tumor lysis syndrome

Intervention	Dosage	Comment
Fluids	3–3.5 L/m^2/day (200 mL/Kg/day if ≤10 Kg)	Exercise caution if congestive heart failure and renal failure
Allopurinol	Oral dose: 50–100 mg/m^2 every 8 h orally (maximum 300 mg/m^2/day) or 10 mg/Kg/day divided every 8 h (maximum 800 mg/day) IV: 200–400 mg/m^2/day in 1–3 divided doses (maximum 600 mg/day)	Drug interaction with thiazide diuretics, ampicillin/amoxicillin 6-mercaptopurine, azathioprine, cyclophosphamide, and methotrexate require dose reduction Renal impairment—50% dose reduction
Rasburicase	IV infusion 0.1–0.2 mg/Kg/day in 50 mL normal saline over 30 min, for 5 days	Contraindicated in glucose-6-phosphate dehydrogenase deficiency Adverse reactions—anaphylaxis, rash, hemolysis, and methemoglobinemia
Sodium bicarbonate	40 to 50 mEq/L should be added to the fluid used for hydration For example, 20 mEq of sodium bicarbonate must be added 500 mL fluid bag	Can worsen hypocalcemia It can also lead to precipitation of calcium and phosphate salts in the renal tubules worsening AKI Alkalinization should be done only if rasburicase is not available
Hyperkalemia	Calcium gluconate: 100–200 mg/Kg by slow IV infusion for life-threatening arrhythmias Albuterol nebulizer Regular insulin: 0.1 U/Kg IV + 25% Dextrose (2 mL/Kg) IV Sodium bicarbonate: 1–2 mEq/Kg IV, push only if pH <7.2 Sodium polystyrene sulfonate: 1 gm/Kg with 50% sorbitol PO/PR Dialysis: if severe	ECG monitoring Avoid PR route in neutropenics Sodium bicarbonate and calcium not to be administered through the same line
Hypocalcemia	Calcium gluconate: 50–100 mg/Kg IV administered slowly or calcium chloride	ECG monitoring
Hyperphosphatemia	Hydration Aluminum hydroxide: 50–150 mg/Kg/day in divided doses PO or through nasogastric tube every 6 h Dialysis: if severe	Limit aluminum hydroxide use to 1–2 days to avoid cumulative aluminum toxicity

Step 4: Start Allopurinol

- Purine catabolism results in the production of hypoxanthine and xanthine, which are metabolized to uric acid via the enzymatic action of xanthine oxidase.
- This pathway can be blocked using allopurinol, a hypoxanthine analog that competitively inhibits xanthine oxidase.
- Start allopurinol PO at 600 mg/day if uric acid is less than 8 mg/dL.
- Allopurinol should be started prior to chemotherapy.

- After about 2–3 days, allopurinol therapy results in increased excretion of both hypoxanthine (more soluble than uric acid) and xanthine (less soluble than uric acid).
- A marked increase in xanthine excretion can occur when allopurinol is given for the prevention of tumor lysis syndrome and may lead to acute renal failure or xanthine stones.
- It should be used cautiously in patients with renal impairment. It has many drug interactions and may cause skin hypersensitivity reactions.
- Febuxostat may be used if the patient is hypersensitive to allopurinol. In the FLORENCE (Febuxostat for TLS Prevention in Hematologic Malignancies) trial, febuxostat had a good safety profile, provided better control of TLS hyperuricemia with preservation of renal functions.

Step 5: Consider Rasburicase (Recombinant Urate Oxidase)

- Urate oxidase—Present in most mammals, but not in humans. It oxidizes preformed uric acid to allantoin, which is 5–10 times more soluble than uric acid in acid urine.
- When exogenous urate oxidase (uricase, rasburicase) is administered, serum and urinary uric acid levels decrease markedly within approximately 4 h.
- This should be used especially if the uric acid level is above 8 mg/dL.
- A single dose of 0.2 mg/kg is recommended.
- Uric acid levels should be monitored regularly to adjust dosing.
- Rasburicase degrades uric acid within the blood samples at room temperature, thus interfering with accurate measurement.
- Therefore, samples should immediately be placed on ice until the completion of assay.
- It should not be given to patients with Glucose 6 phosphate dehydrogenase deficiency due to the risk of severe hemolysis.
- If urgent administration is needed and G 6 PD results are not available, rasburicase can be given at a single low dose of 0.02–0.05 mg/kg up to a maximum of 3 mg.

Step 6: Alkalinization of the Urine

- Alkalinization of urine increases the solubility of uric acid by 10 times. This was recommended earlier but is controversial as it can lead to the formation of urinary xanthine crystals and precipitation of calcium and phosphate salts in the renal tubules worsening AKI.
- This may cause obstruction of renal tubules if allopurinol is used concurrently.
- It is not recommended with recombinant urate oxidase (rasburicase).
- Monitor ionized calcium level.

Step 7: Administer Calcium

- If asymptomatic hypocalcemia, no therapy is required.
- Calcium gluconate and calcium chloride can be administered intravenously.

However, it can increase the deposition of calcium phosphate crystals in the kidneys and may worsen AKI.

Step 8: Consider Hemodialysis

- Best modality for removal of solutes.
- This modality should be considered in specific situations such as
  - Uncontrolled/life-threatening hyperkalemia and severe hyperphosphatemia
  - Volume overload
  - Uric acid of more than 10 mg/dL despite rasburicase
  - Renal failure

Step 9: Use Diuretics Cautiously

- Maintain adequate urine output.
- It is contraindicated if hypovolemia or obstructive uropathy exists.

Step 10: Treat Associated Electrolyte Disorders

- Hyperphosphatemia—restrict phosphate intake and increase loss with phosphate binders such as aluminum hydroxide or calcium carbonate, sevelamer hydroxide, and lanthanum carbonate.
- Hyperkalemia and hypocalcemia (Table 12.2).

Superior Vena Cava Syndrome

A 19-year-old patient with lymphoma presented with dyspnea, swelling of the head and the neck, and upper limbs, and distended veins on the neck and the upper chest.

Superior vena cava syndrome (SVCS) is a compendium of clinical signs and symptoms due to partial or complete obstruction of venous return through the superior vena cava, which results in increased upper body venous pressure. It is most commonly due to malignancy. The majority of cases are due to lung cancer or non-Hodgkin lymphoma.

Step 1: Resuscitate
Compression of the tracheobronchial tree causing airway compromise is an airway emergency, needing intubation (with a small endotracheal tube) and ventilation till definitive treatment (refer Chap. 24). Give a propped-up position to elevate the head of the patient. Anticipate difficult airways, including difficult mask ventilation, laryngoscopy, and intubation. Follow the difficult airway algorithm.
Step 2: Do imaging
Computed tomography (CT) chest scan with or without venography is diagnostic. These patients may not be able to lie supine for CT chest. They must be intubated before CT or empirical therapy needs to be started. Doppler extremity venogram or duplex ultrasound for patients with a central venous catheter in the upper extremity to exclude venous thrombus.
Step 3: Confirm diagnosis
Obtain a biopsy before instituting therapy if the diagnosis is uncertain. Proper hemostatic measures should be taken while performing invasive procedures.
Step 4: Chemotherapy and corticosteroids
These can be administered, especially in chemosensitive tumors.
Step 5: Radiotherapy
This is a standard treatment modality for sensitive tumors but may take a few weeks to show effect.
Step 6: Stenting of the superior vena cava
It is effective and feasible in relieving the symptoms of superior vena cava syndrome. If SVCS is secondary to thrombus following an indwelling intravascular device, consider removing the device along with anticoagulation therapy and catheter-directed thrombolysis.

Malignant Spinal Cord Compression

A 68-year-old patient with carcinoma of the prostrate developed worsening back pain progressively with radiating pain down the right leg associated with weakness, difficulty in walking, and loss of bladder and bowel function.

Acute spinal cord compression is an emergency. It can be caused by tumors of the spinal cord or vertebral or extradural metastases from other tumor sites.

Step 1: Resuscitate (see Chap. 24*)*
(a) Pain relief with adequate analgesics is a priority in these patients. (b) Urgent neurosurgical, radiotherapy, and oncology consultation for limb salvage is necessary. (c) Take special precautions while transporting these patients.

(continued)

Step 2: Consider imaging and other laboratory tests

In patients with a high index of suspicion and symptoms suggestive of metastatic bone disease, magnetic resonance imaging is the gold standard for diagnosis.
Alternatively CT scan of the spine should be done
It is important to image the entire spine as more than one area of compression may be present.
Look for hypercalcemia as it is a common metabolic derangement in patients with malignancy.
Alkaline phosphatase is a marker of bone turnover and mineralization. Elevated levels are seen in patients with bone metastasis.

Step 3: Start glucocorticoids

Corticosteroids should be initiated as early as possible preferably within 12 h of onset of symptoms. Dexamethasone is indicated in patients with motor deficits or radiologic evidence of neural compression.
It is given as an initial intravenous dose of 10–16 mg followed by 4 mg every 4 h.
This is later administered orally and tapered over 10–12 days.
Use proton pump inhibitors or H_2 blockers along with a high dose of corticosteroids.

Step 4: Consider radiation therapy

This has been the mainstay of the treatment in patients with and without motor deficit particularly in radiosensitive tumors (e.g., small cell lung carcinoma and myeloma).
This is usually combined with surgery for spine stabilization.

Step 5: Consider surgery

It is indicated in most cases, especially in patients with a good performance status. Indications of surgery are the following:

- Gross instability of the spine
- Rapidly progressive symptoms
- Progressive symptoms during radiation therapy
- When tissue diagnosis is needed
- Radioresistant tumors

Step 6: Consider chemohormonal therapy

Hormonal chemotherapy and zoledronic acid should be considered in sensitive tumors such as prostate cancer, testicular tumor, or lymphoma.

Suggested Reading

Abrahm JL. Assessment and treatment of patients with malignant spinal cord compression. J Support Oncol. 2004;2:377–401A. *Very comprehensive evidence-based review on malignant spinal cord compression*

Adeyinka A, Bashir K. Tumor lysis syndrome. [Updated 2022 Oct 31]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024. Available from: https://www.ncbi.nlm.nih.gov/books/NBK518985/.

Coiffier B, Altman A, Pui CH, Younes A, Cairo MS. Guidelines for the management of pediatric and adult tumor lysis syndrome: an evidence-based review. J Clin Oncol. 2008;26:2767–78.

Coiffier B, Altman A, Pui CH, Younes A, Cairo MS. Guidelines for the management of pediatric and adult tumor lysis syndrome: an evidence-based review. J Clin Oncol. 2008;26(16):2767–78. https://doi.org/10.1200/JCO.2007.15.0177. Erratum in: J Clin Oncol. 2010 Feb 1;28(4):708

Halfdanarson TR, Hogan WJ, Moynihan TJ. Oncologic emergencies: diagnosis and treatment. Mayo Clin Proc. 2006;81(6):835–48. www.mayoclinicproceedings.com. *This review covers the complete spectrum of oncological emergencies with their etiopathogenesis and initial therapy. A must read for those caring for cancer patients. It does not require subscription*

Web Links

Vakiti A, Anastasopoulou C, Mewawalla P. Malignancy-related hypercalcemia. [Updated 2023 Apr 16]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024. Available from: https://www.ncbi.nlm.nih.gov/books/NBK482423/.

http://emedicine.medscape.com/article/766373-treatment

www.mayoclinicproceedings.com

Part III

Trauma and Burn

General Management of Trauma

13

Babita Gupta, Yash Javeri, Deepak Govil,
and Praveen Kumar

A 30-year-old male patient hit by a car about 3 h ago presented in the hospital. On arrival at the hospital, he had labored breathing; his respiratory rate was 30/min with O_2 saturation of 95% on room air. His heart rate was 132/min, blood pressure was 105/80 mmHg, and Glasgow coma score (GCS) was 8/15. After initial stabilization, the secondary survey revealed multiple rib injuries on the left side of the chest and a fracture of the left femur.

Trauma is a major cause of death and disability in the first four decades of life. Improvement and organization of trauma care services are a cost-effective way of improving patient outcomes. Proper organization of these systems reduces the time between injury and definitive care, thereby reducing morbidity and mortality.

While managing injured patients, since timing is critical, a systematic approach that can be expeditiously and accurately applied is vital. Advanced Trauma Life Support (ATLS®) principles guide the initial management of a trauma victim. This systematic approach, termed "initial assessment," includes the following elements.

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Step 1: Preparation

Crucial steps of preparation in the hospital include

- Alert the trauma team about the arrival of the injured patients and the number of causalities so that rapid resuscitation can be initiated.
- Trauma team includes the general/trauma surgeon, the emergency physician, the orthopedic surgeon and the critical care/anesthesia specialist on call, and at least two trained nurses and two paramedics.
- Besides the surgeon, the trauma team can also be led by an emergency medicine or critical care/anesthesia specialist who is skilled in airway management.
- Alert the imaging, laboratory services, blood bank, and operating room personnel about the arrival of a polytrauma patient.
- Airway cart, crash cart, suction, monitors and IV cannula, warm IV fluids, and other equipment should be rechecked.
- The team members should be ready with universal precautions by putting on masks, splash-resistant and lead gowns, eye protection, and gloves.
- If the patient has been shifted in an ambulance with a paramedic/medic, proper hand-over from the prehospital providers should be done and all important information should be shared with the receiving team.
- In case mass/multiple casualties is expected, preparation/alerts should be made as per predefined institute protocol, which is prepared as per available resources.

Step 2: Triage

- Triage is a process of determining the priority of treatment based on the patient's airway (A), breathing (B), and circulation (C) as well as availability of resources.
- Injured patients can be categorized into five categories:
    1. The injured patient with compromised ABC who requires immediate life-saving intervention (red)
    2. The injured patient with stable ABC but requires further investigation and/or observation (yellow)
    3. Those with minor injuries (walking wounded), who need help less urgently (green)
    4. The unsalvageable patients who are beyond help (blue or gray)
    5. The injured patients who are already dead (black)
- A simple tool that can be used for triage is START (simple triage and rapid treatment) (Fig. 13.1).

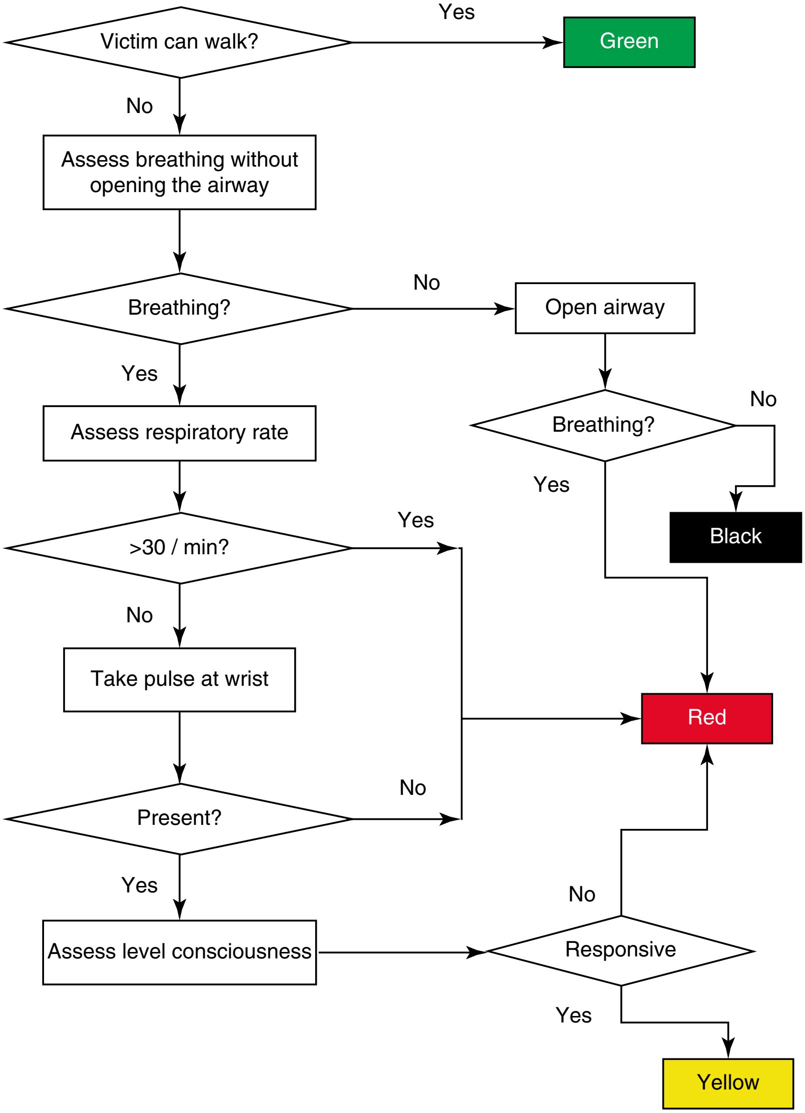
Victim can walk?
Yes
Green
No
Assess breathing without opening the airway
Breathing?
No
Open airway
Yes
Assess respiratory rate
Breathing?
No
Yes
Black
>30 / min?
Yes
No
Take pulse at wrist
Red
Present?
No
Yes
No
Assess level consciousness
Responsive
Yes
Yellow

Fig. 13.1 Simple triage and rapid treatment

Step 3: Primary Survey with Simultaneous Resuscitation

The "ABCDE" of the primary survey is, in essence, to identify injuries with immediate threat to life and institution of life-saving interventions systematically. The ABCDE comprises of

- Airway maintenance with restriction of cervical spine motion
- Breathing and ventilation
- Circulation with hemorrhage control
- Disability (assessment of neurological status)
- Exposure/environmental control
  - The management is concurrent with the assessment, resuscitation, and stabilization.
  - A 10-s assessment tool that can rapidly assess patients' ABCD is: Ask the patient to identify himself and narrate the incident. A patient with normal and clear speech and a normal level of consciousness is unlikely to have a major compromise in ABCD and unlikely to have a major event immediately.
  - Take a history from the accompanying person about the following:
    Mechanism of injury
    Injuries suspected
    Vital signs
    Treatment en route to hospital
  - Detailed history should not interfere with primary survey, identification, and treatment of life-threatening injuries.

A. Airway with restriction of cervical spine motion
  - The airway is assessed immediately for patency, protective reflexes, foreign body, secretions, and injury and burns.
  - The patency of the airway should be assessed with special attention to foreign body or maxillofacial fractures and laryngeal injuries that may result in airway obstruction.
  - Absence of response, stridor, confusion, or a hoarse reply may indicate airway compromise.
  - Chin-lift or jaw-thrust maneuver may be used to achieve airway patency, simultaneously protecting the cervical spine, either by a semirigid cervical collar or by manual inline stabilization by a team member.
  - Head tilt maneuver should be avoided in an injured patient while managing the airway.
  - A definitive airway is required in the following conditions*:*
    - Inadequate ventilation and oxygenation
    - Impending or actual airway obstruction secondary to injury
    - Brain injury with a GCS of ≤8
    - Inability to adequately protect the airway from aspiration
    - Severe multisystem injury or hemodynamic instability
    - Facial burns or inhalation injury

    - Inability to closely monitor during ongoing resuscitation and investigation (e.g., angiography and CT scanning)
    - Uncooperative or combative behavior of the patient
  - Cervical spine protection (by application of cervical collar or manual restriction) during airway maneuvers should be done in all trauma patients unless specifically cleared for cervical spine injury preferably by a neurosurgeon.
  - Three-person intubation technique should be followed in all trauma patients.
  - Drug-assisted intubation protocol should be followed in all trauma patients for securing airway.
  - Ketamine 1–2 mg/kg or etomidate 0.2–0.3 mg/kg along with 1–2 mg/kg succinylcholine is used, depending on the hemodynamic stability.
  - Succinylcholine should be used with utmost caution in patients with preexisting neuromuscular diseases or paralysis, renal failure, and in patients with major crush injuries, burns, and electrical injuries as this can worsen potassium levels.
  - Difficult or failed intubations
    - Call a senior anesthesiologist or a more experienced person in airway management
    - Anticipate airway problems with the following:
      - Injury to cervical spine
      - Maxillofacial and neck trauma
      - Facial and inhalational burns
      - Obesity
      - Variations in anatomy
  - Airway management options with cervical spine protection include
    - Oxygen administration.
    - Basic airway maneuvers: chin lift and jaw thrust (no head tilt).
    - Oropharyngeal or nasopharyngeal airway, with caution in bleeding and conscious patient. Avoid nasopharyngeal airway insertion in patients with suspected base of skull fracture.
    - Adjuvants: Bougie, stylet, laryngeal mask airway, laryngeal tube airway, and intubating LMA.
    - Endotracheal intubation.
    - Surgical airway, that is, needle or surgical cricothyroidotomy if unable to intubate.
  - Percutaneous tracheostomy is not recommended in emergency trauma situations.

B. Breathing and ventilation
  - Chest wall mechanics are altered due to rib fractures, pulmonary contusions, and cervical spinal cord injury.
  - Breathing is assessed by determining the patient's respiratory rate and by subjectively quantifying the depth and effort of inspiration.
  - The patient's chest should be exposed to adequately assess chest wall excursion.

- Identify injuries that hamper ventilation by rapid but thorough physical examination. Injuries that need to be identified and managed during the primary survey are
  - Tension pneumothorax (hyper-resonance on percussion with midline shift)
  - Massive hemothorax (dullness on percussion)
  - Tracheobronchial injuries (crepitus on palpation)
  - Open pneumothorax (sucking chest wound)
  - Cardiac tamponade (muffled heart sounds, Kussmaul's breathing)
- If tension pneumothorax is identified, immediate needle decompression in the fifth intercostal space in mid-axillary line should be performed, followed by intercostal tube drainage.
- Needle decompression in the second intercostal space is no longer recommended as a first choice.
- Rapid respiratory effort, use of accessory muscles of respiration, hypoxia, hypercapnia, asymmetric chest wall excursions, and diminished or absent breath sounds will require treatment before proceeding further.
- *Breathing—treatment options include*
  - Endotracheal intubation and ventilation
  - Needle decompression followed by chest drain
  - Three-sided sterile occlusive dressing for open pneumothorax
  - Intercostal tube drain
  - Thoracotomy if blood loss>1500 mL on chest drain insertion or continuous blood loss, that is, >200 mL/h for 2–4 h
  - Adequate analgesia

C. Circulation with hemorrhage control
   - Hypotension in a trauma patient is always assumed to result from significant hemorrhage (>30% blood loss), once tension pneumothorax is ruled out.
   - Rapid and accurate assessment of the patient's hemodynamic status and identification of the site of hemorrhage is therefore essential.
   - It is critical to establish two large-bore short-length intravenous cannulas (16G or wider) in a trauma patient, preferably in the upper extremities, and resuscitation should be started with one-liter warm crystalloids.
   - All patients with significant hemorrhage should receive Tranexemic acid within 3 h of trauma (1gm bolus followed by 1gm over 8 h).
   - Blood and blood products transfusion should be done in patients with ongoing hemodynamic instability after initial fluid boluses, preferably in the ratio of 1:1:1 (PRBC:FFP:platelets). Group 0 RBC and AB plasma may be administered in exsanguinating hemorrhage if crossmatched RBC and plasma is unavailable except in females of childbearing age.
   - Colloids should not be used in hemorrhagic shock.
   - All patients requiring massive transfusion should be identified early by using simple scores like Trauma-Associated Severe Hemorrhage (TASH) and Assessment of Blood Consumption (ABC) score.
   - Point-of-care assessment for coagulopathy by thromboelastography (TEG) or other viscoelastic test should be done if available.

- All steps to prevent the lethal triad, that is, hypothermia, acidosis, and coagulopathy should be initiated.
- Look for blood in five places: chest, abdomen, pelvis, long bones, and floor (for missed bleeding source).
- Chest and pelvic radiographs and an extended focused assessment by sonography in trauma (eFAST) should be done in all trauma patients. Diagnostic peritoneal lavage (DPL) can be considered in select patients if ultrasound is not available.
- Diagnostic peritoneal lavage should not be considered in patients with morbid obesity, previous abdominal surgeries, coagulopathy, and advanced liver cirrhosis.
- Hemorrhage control by direct application of external pressure and/or careful application of a tourniquet may be done in all patients. Tourniquets should be left in place till the bleeding is controlled surgically, but the time should be limited.
- The pelvic ring should be closed using pelvic binders if the bleeding is suspected from an unstable pelvis. A simple sheet can be used if the commercial pelvic binder is not available.
- Fractured long bones should be reduced, and traction splint applied if they are a possible source of bleeding to decrease ongoing blood loss and pain as well as to prevent further local injury.
- Damage control resuscitation should be considered in all hemodynamically unstable trauma patients due to hemorrhagic shock.
- Repeated reassessment should be carried out to identify initial responders who would eventually become nonresponder.
- Hypotension generally does not manifest until at least 30% of blood volume has been lost.
- In very elderly, features of hypoperfusion may not present with obvious manifestations.
- *Circulation and hemorrhage control—treatment options include*
  - Two large-bore IV cannulas (16G or bigger)
  - Warm fluids (crystalloids)
  - Warm blood and blood products
  - Early use of tranexamic acid
  - eFAST for early identification of the source
  - Arrest bleeding by direct local pressure and tourniquets
  - Arrest bleeding by splinting the pelvis and long bones
  - Urinary catheter
  - Surgery—laparotomy, thoracotomy, and/or pelvic fracture fixation should be undertaken to control bleeding
  - Repeated assessments

D. *Disability/neurological status*

- A rapid neurological evaluation is carried out at the end of the primary survey only after resuscitation and stabilization have been achieved as mentioned above.

- This assesses the patient's level of consciousness, pupillary size and reaction, and focal neurological deficit.
- The level of consciousness may be described in terms of the GCS.
- The GCS is used as a baseline determination of neurological function, and frequent reassessment is required to detect an early or previously missed injury.
- Hypoglycemia, drug, and alcohol intoxication should be considered for altered consciousness, but all trauma patients with altered GCS have brain injury unless proven otherwise.
- A complete neurological examination is not appropriate at this time and should be performed during the secondary survey.
- Adequate oxygenation and perfusion should be maintained to prevent secondary brain injury.
- *Disability—treatment options include*
  - O_2 administration
  - Intubation (to ensure normal PaO_2 and $PaCO_2$)
  - Avoid hypotension and hypoxia to prevent secondary brain damage
  - Inotropes/vasopressors (to ensure adequate cerebral perfusion)
  - Head up, ensure venous drainage
  - Emergency imaging of the brain or spine
  - Early neurosurgical consultation

E. *Exposure/environmental control*

- The patient should be completely undressed to facilitate thorough examination and assessment in the front and back.
- At the same time, care should be taken to prevent hypothermia.
- Remove wet or blood-soaked clothes, and use warm IV fluids (39 °C).
- Use blood warmers for transfusing and external warming (warmed blankets to all patients and forced, heated air, or radiant warmers as needed) to prevent hypothermia.

Step 4: Adjuncts to Primary Survey and Resuscitation

(a) *ECG monitoring*

- The appearance of dysrhythmias may indicate blunt cardiac injury.
- Pulseless electrical activity, the presence of cardiac rhythm without a peripheral pulse, may indicate cardiac tamponade, tension pneumothorax, or profound hypovolemia.
- Extreme hypothermia can also be the cause of cardiac rhythm disturbances.

(b) *Urinary catheter*

- Urine output is a sensitive indicator of the volume status of the patient and reflects renal perfusion and adequacy of resuscitation.
- All trauma victims should be catheterized to enable monitoring of the urine output and plan intravenous fluid therapy.

  - Transurethral catheterization is contraindicated in patients for whom urethral transaction is suspected (presence of blood in meatus or perineal ecchymosis).

(c) *Gastric catheter*

  - A nasogastric tube is indicated to reduce stomach distension and decrease the risk of aspiration. An orogastric is preferred in patients with skull base fractures.

(d) *X-rays and diagnostic studies*

  - The chest and pelvis X-rays help in the assessment of a trauma patient.
  - The blood should be sent for crossmatching and arranging for packed cells, and important diagnostic parameters such as hemoglobin, coagulation profile, renal parameters, electrolytes, random blood sugar, and arterial blood gas (ABG) should be checked.
  - Pulse oximetry is a valuable adjunct for monitoring oxygenation and adequacy of peripheral circulation in injured patients.

(e) e*FAST (extended focused assessment with sonography for trauma)*

  - The FAST is a rapid, bedside, ultrasound examination performed to identify intraperitoneal hemorrhage or pericardial tamponade. FAST examines four areas for free fluid: perihepatic and hepatorenal space, perisplenic, pelvis, and pericardium.
  - eFAST helps in identifying pneumothorax and hemothorax.

Step 5: Consideration for Interhospital Transfer

- Identify the early, potential need for transfer of the polytrauma patient to an institution where definitive care can be undertaken.
- Transfer decision should be based on known injuries and patterns of injury.
- Effective communication, including the condition of the patient, treatment given, and anticipated requirements during transfer, should be made to the receiving hospital.

Step 6: Admit in the ICU

- Airway protection and mechanical ventilation
- Requirement of inotropes/vasopressors
- Severe head injury
- Organ support
- Correct coagulopathy
- Invasive monitoring
- Active rewarming of hypothermic patients
- Requirement of resurgery

- Brain-dead patient scheduled for organ retrieval
- Observation in solid organ injury or aortic injury requiring endovascular repair
- ECG changes in patient with suspected blunt cardiac injury

Step 7: Secondary Survey

- Once the primary survey is accomplished—life-threatening conditions are managed and resuscitative efforts are underway—secondary survey is carried out.
- This is a head-to-toe evaluation of the trauma patient, which includes a complete history and physical examination and reassessment of all the vital signs.
- History includes the following:
  - A—allergies
  - M—medications currently taken
  - P—past illness/pregnancy
  - L—last meal
  - E—events/environment related to the injury
- Each region of the body is completely examined.
- The care should be continued with regular re-evaluation of the patient for any deterioration and new findings so that appropriate measures can be taken.

Re-evaluation

- After the completion of the secondary survey, the patient should be reevaluated beginning with the ABCs and thorough physical examination and examined for any missed injury (tertiary survey) such as fractures.
- Constant monitoring of the severely injured patient is required and may necessitate rapid transfer to the surgical intensive care unit, operating room, or to another center having better-specialized facilities.
- Appropriate referrals for specialists should be sent.
- Adequate pain relief, tetanus prophylaxis, and antibiotics should be given.
- Specific care should be taken to examine the possible missed injuries on the following:
  - Back of the head and the scalp
  - Neck, beneath semirigid collar
  - Back, buttocks, and flanks
  - Groin creases, perineum, and genitalia

Step 8: Sending Investigations

- Hemoglobin
- Hematocrit
- ABG
- Renal function tests and electrolytes
- Blood sugar

- Total leukocyte count
- Platelet count
- Liver function tests and coagulation tests
- Blood grouping and cross-matching
- Urine pregnancy test (14–45 years)
- ECG
- Breath/blood alcohol

Radiological
- Plain radiographs
- CT scanning
- Contrast studies
- Angiography
- Ultrasound (including plain sonography echocardiography and color flow Doppler)
- Endoscopy

Step 9: Tertiary Survey

- Tertiary survey consists of a repeat of the primary and secondary survey examinations, reassessment of the functions of all tubes and catheters, and review of all X-rays.
- It is routinely performed in the morning after the patient's admission to detect any injuries not picked up earlier to minimize the missed injuries.

Suggested Reading

American College of Surgeons Committee on Trauma. Initial assessment and management. Advanced trauma life support program for doctors. 10th ed. *Comprehensive text in context with advanced trauma life support (ATLS) program.*

Babita G, Yudhyavir S, Dinesh B, Abhishek N. Comprehensive management of the patient with traumatic cardiac injury. Anesth Analg. 2023;136(5):877–93. *This article explains the algorithm of the management of penetrating and blunt cardiac injury*

Moore EE, Feliciano DV, Mattox KL, editors. Trauma. 5th ed. New York: McGraw-Hill; 2004.

Sahu AK, Bhoi S, Galwankar S, Aggarwal P, Murmu L, Nayer J, Sinha TP, Mishra PR, Ekka M, Kumar A. All India Institute of Medical Sciences Triage Protocol (ATP): ATP of a Busy Emergency Department. J Emerg Trauma Shock. 2020;13(2):107–9. *This article explains the basis of triage of trauma victims*

Stiell IG, Clement CM, et al. The Canadian C-spine rule versus the NEXUS low-risk criteria in patients with trauma. N Engl J Med. 2003;349:2510–8. *This article explains the basis of early management of cervical spine injuries*

Spahn DR, Bouillon B, et al. The European guideline on management of major bleeding and coagulopathy following trauma: fifth edition. Crit Care. 2019;23(1):98. *Guidelines for the management of bleeding and coagulopathy during trauma*

14

Traumatic Brain and Spinal Injury

Kapil Zirpe and Balkrishna Nimavat

A 25-year-old adult had an alleged history of bike skid. On arrival at the emergency department, he was found to be unconscious with bleeding from the scalp. The patient had a history of vomiting twice. His pulse rate was 60/min, and his blood pressure was 140/80 mmHg. The pupillary size showed asymmetry, and his breathing was labored.

Traumatic brain injury (TBI) is the leading cause of mortality and morbidity in children and young adults in both developed and developing nations worldwide. The aims and objectives of its management are prompt management of intracranial hypertension and secondary brain injury, maintenance of cerebral perfusion pressure, and ensuring adequate oxygen delivery to the injured brain tissue (Fig. 14.1).

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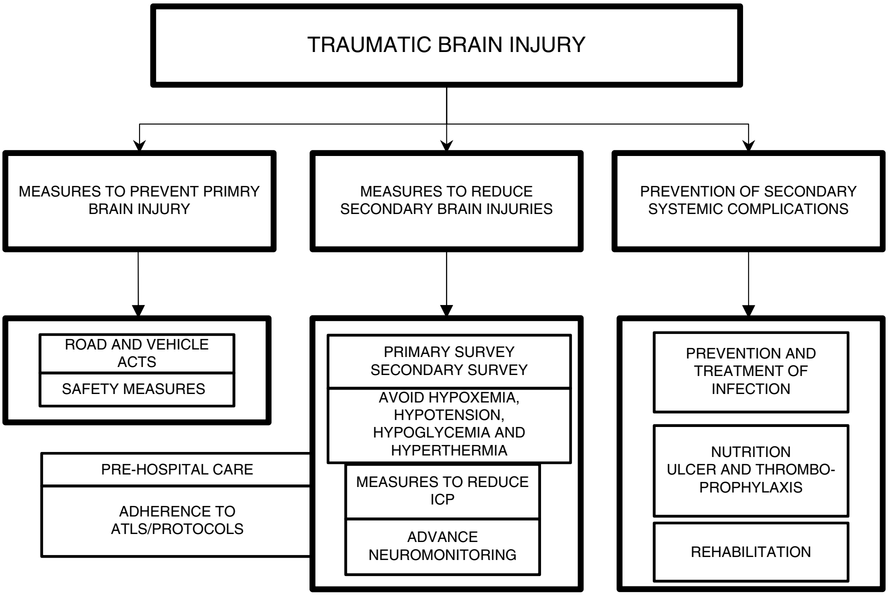
TRAUMATIC BRAIN INJURY
MEASURES TO PREVENT PRIMRY BRAIN INJURY
MEASURES TO REDUCE SECONDARY BRAIN INJURIES
PREVENTION OF SECONDARY SYSTEMIC COMPLICATIONS
ROAD AND VEHICLE ACTS
SAFETY MEASURES
PRE-HOSPITAL CARE
ADHERENCE TO ATLS/PROTOCOLS
PRIMARY SURVEY SECONDARY SURVEY
AVOID HYPOXEMIA, HYPOTENSION, HYPOGLYCEMIA AND HYPERTHERMIA
MEASURES TO REDUCE ICP
ADVANCE NEUROMONITORING
PREVENTION AND TREATMENT OF INFECTION
NUTRITION ULCER AND THROMBO-PROPHYLAXIS
REHABILITATION

Fig. 14.1 Management objectives for TBI

Traumatic Brain Injury

Step 1: Initial Assessment/Components of Primary Survey

Airway Control and Ventilation

Airway, breathing, and circulation take precedence despite obvious head injury.

- Secure cervical spine with a cervical collar: An unstable cervical spine injury can occur in 5–6% of cases of TBI. Risk factors include a motor vehicle collision, assaults, falls, and a GCS of less than 8.
- In suspected cervical spine injury, orotracheal intubation, and ventilation with 100% oxygen along with manual inline cervical immobilization with the cervical collar off to reduce the chance of worsening a neurological injury until the radiological clearance is obtained.
- Prevent hypoxemia: Avoid PaO_2 less than 80 mmHg or O_2 saturation below 94%.
- Consider rapid sequence intubation: Succinylcholine or rocuronium may be used as a muscle relaxant. Although succinylcholine may produce a small increase in ICP, this has not proven to be clinically significant. To facilitate intubation an opiate such as fentanyl (1–2 microgram/kg) may be used, there is no evidence to support the use of lidocaine during intubation.

- Adequate sedation and muscle relaxation tend to reduce the cerebral metabolic oxygen requirement ($CMRO_2$), optimize ventilation, and prevent coughing or straining.
- Choice of sedative agent: Anesthetic drugs that allow for rapid control of the airway while avoiding an increase in intracranial pressure (ICP) and providing hemodynamic stability are preferred. Propofol and thiopental are the most commonly used drugs, but they may cause hypotension. Etomidate has advantages in terms of cardiovascular stability, but the possibility of adrenal suppression exists. Ketamine is popular in trauma patients and recent evidence suggests that its effect on ICP may be limited.
- Ventilator strategy:
  1. Hypoventilation should be avoided as increased PCO_2 levels may lead to cerebral hyperemia with an increase in blood volume and ICP.
  2. Hyperventilation, on the other hand, results in an increased risk of vasoconstriction and increased tissue hypoxia, especially in the penumbra zone, so it is best avoided. CO_2 level should be kept at 35–45 mmHg and use of end tidal CO_2 monitor in most intubated patients.
  3. The ventilator should be adjusted to achieve a PaO_2 of ~60 mmHg, which can oxygenate the penumbra zone. High PaO_2 should be avoided considering the risk of hyperoxic cerebral vasoconstriction. PEEP of 5–10 cm H_2O may be administered to prevent atelectasis and has been proven to be safe in these patients.
  4. Hyperventilation up to a $PaCO_2$ between 28 and 35 mmHg for the purpose of reducing ICP is recommended for a brief period to avoid brain herniation (not less than 30 mmHg).
  5. Give a single dose of ceftriaxone 2 gm intravenously in patients with TBI who require endotracheal intubation to decrease the risk of ventilator-associated pneumonia.

Blood Pressure and Cerebral Perfusion Pressure (CPP)

- Maintain systolic blood pressure >100 mm Hg in patients with 50–69 years old, and >110 mm Hg in patients 15–49 years or >70 years old.
- In a hypotensive TBI patient, hypovolemia resulting from noncranial hemorrhage should be ruled out.
- Choice of fluid: Hypotonic solutions like 5% dextrose should be avoided. Isotonic normal saline is the most common crystalloid used in TBI patients, but Ringer's lactate or other balanced crystalloids are an alternative and result in less acute kidney injury. Infusion of large volumes of normal saline results in adverse hyperchloremic metabolic acidosis that is detrimental to TBI. On the other hand, balanced crystalloids are relatively hypotonic and may exacerbate cerebral edema.
- Colloids appear to provide no further benefit.
- Saline is preferable to albumin resuscitation as the latter has been found to increase mortality in TBI patients.

- The recommended target CPP (MAP-ICP) value for survival and favorable outcomes is between 60 and 70 mmHg.
- Vasopressors are commonly used to augment CPP in the setting of TBI but avoid aggressive attempts to maintain CPP above 90 mmHg with fluids and pressors (if no invasive monitoring tool is available).
- Labetalol is the drug of choice for the control of hypertensive emergencies in TBI.

Step 2: Secondary Survey/Neurological Assessment

Neurological Assessment

- The Glasgow coma scale (GCS) has been the most widely used method of recording the level of consciousness in patients at presentation and at subsequent assessment. A score of ≥13 correlates with a mild brain injury, 9–12 is a moderate injury, and ≤8 is a severe brain injury.
- Patients with a Glasgow coma scale ≤13 and moderate to severe extracranial anatomical injuries should be rapidly transferred to a higher level of care.
- TBI can be classified based on severity and morphology (Table 14.1).

Step 3: Do Imaging—CT Scan

- Indications of CT in TBI: a CT scan brain should be carried out in all moderate-to-severe TBI.
- For mild TBI, CT scan indications are
  1. Open or depressed skull fracture
  2. Sign of basilar skull fracture
  3. Vomiting more than two episodes
  4. Age >65 years
  5. Anticoagulant use
  6. Seizure

Table 14.1 Classification of TBI

Based on severity (GCS)	Mild	13–15	
	Moderate	9–12	
	Severe	<9	
Based on morphology	Skull fractures	Vault	Linear vs. stellate/compound
			Depressed/nondepressed
		Basilar	With/without CSF leak
			With/without cranial nerve palsy
	Intracranial lesions	Focal	EDH, SDH Intracerebral
		Diffuse	Hypoxic/ischemic injury Diffuse axonal injury Multiple contusion Concussion

Step 4: Monitoring of Intracranial Pressure (ICP) and Measures to Reduce ICP

ICP Monitoring and Management

- ICP monitoring is important, but it does not replace careful neurological and radiological examination. ICP should be monitored in patients with GCS of 3–8.
- ICP should also be monitored in patients with severe traumatic head injury with a normal CT scan if the patient is above 40 years, unilateral or bilateral motor posturing, or systolic pressure less than 90 mmHg.
- Patients with elevated ICP have been shown to have worse outcomes and are at a higher risk of mortality.
- Management of severe TBI patients based on ICP monitoring may reduce in-hospital and 2-week post-injury mortality.
- Clinical judgment should be used to initiate intracranial monitoring in patients who are at a high risk of clinical deterioration.
- It is recommended to treat ICP > 22 mmHg to reduce mortality.
- For patients with TBI, maintaining monitored intracranial pressure by parenchymal ICP tool at 20 mm Hg or less was not superior to care based on imaging and clinical examination (BEST-TRIP trial).

Initial measures of raised ICP include head of bed elevation, keeping neck in neutral position appropriate sedation and analgesia, osmotherapy, and removal of CSF.

Sedation and Analgesia

- Sedatives and analgesics can affect outcomes in head-injured patients.
  - Adequate pain control and sedation (Analgo-sedation) can be used as initial measures to control raised ICP.
  - Short-acting agents such as fentanyl, midazolam, or propofol are preferred for frequent neurological assessments (Table 14.2). High-dose barbiturates are recommended to control ICP refractory to maximum standard surgical and medical treatments while ensuring hemodynamic stability.

    Hemodynamic stability is essential before and during barbiturate therapy. Although propofol may be used for ICP control, it is not recommended for

Table 14.2 Drugs and doses of sedatives and analgesics

Commonly used sedatives	
Fentanyl	2 mcg/kg test dose, 2–5 mcg/kg/h continuous infusion
Midazolam	2 mg test dose, 2–4 mg/h continuous infusion
Sufentanil	10–30 mcg test bolus, 0.05–2 mcg/kg continuous infusion
Propofol	0.5 mg/kg test bolus, 20–75 mcg/kg/min continuous infusion (not to exceed 5 mg/kg/h)

improvements in mortality or 6-month outcomes. Despite optimal sedation and analgesia if ventilatory dyssynchrony (responsible for high ICP and compromised CPP), advisable to give trial dose of neuromuscular paralytic agent. It is well demonstrated that infusion of paralytic agent only started once a positive response is observed.

Start Osmotherapy (Fig. 14.2)

- Osmotherapy with mannitol or hypertonic saline has been used for many years but controversy remains regarding which solution is the best agent and regarding the best method of administration.
- Mannitol is used more often as intermittent boluses (0.25-1gm/kg). It should be stopped if serum osmolality exceeds 320 mOsm/L. It should be avoided in hypovolemia and renal failure patients. Hypertonic saline as intermittent boluses of 3% 250 mL over half an hour or 30 mL of 23.4% can also be used. Withhold if sodium exceeds 155 mEq/L. Serum sodium and osmolality must be assessed every 6 hourly.
- No specific hyperosmolar treatment protocol is superior.

Surgical Options and TBI

Acute hematoma with rapidly progressive neurological deterioration (difference between EDH and SDH + indication of surgery in acute EDH and SDH mentioned in Table 14.3), disappearance of basal or peri-mesencephalic cisterns, and high ICP despite optimal medical intervention are indication of surgery in TBI.

Decompressive Craniectomy

- Decompressive craniectomy is a surgical procedure that involves removal of a large section of the skull. Craniectomy reduces ICP by giving extra space to the swollen brain, and it may quickly prevent brainstem herniation.
- Decompressive craniectomy may be a life-saving surgery, but it comes at the expense of higher chances of severe disability among survivors (RESCUEicp trial).
- Guidelines recommend a large frontotemporoparietal decompressive craniectomy, as opposed to a smaller one, to target reduced mortality and better neurological outcomes.

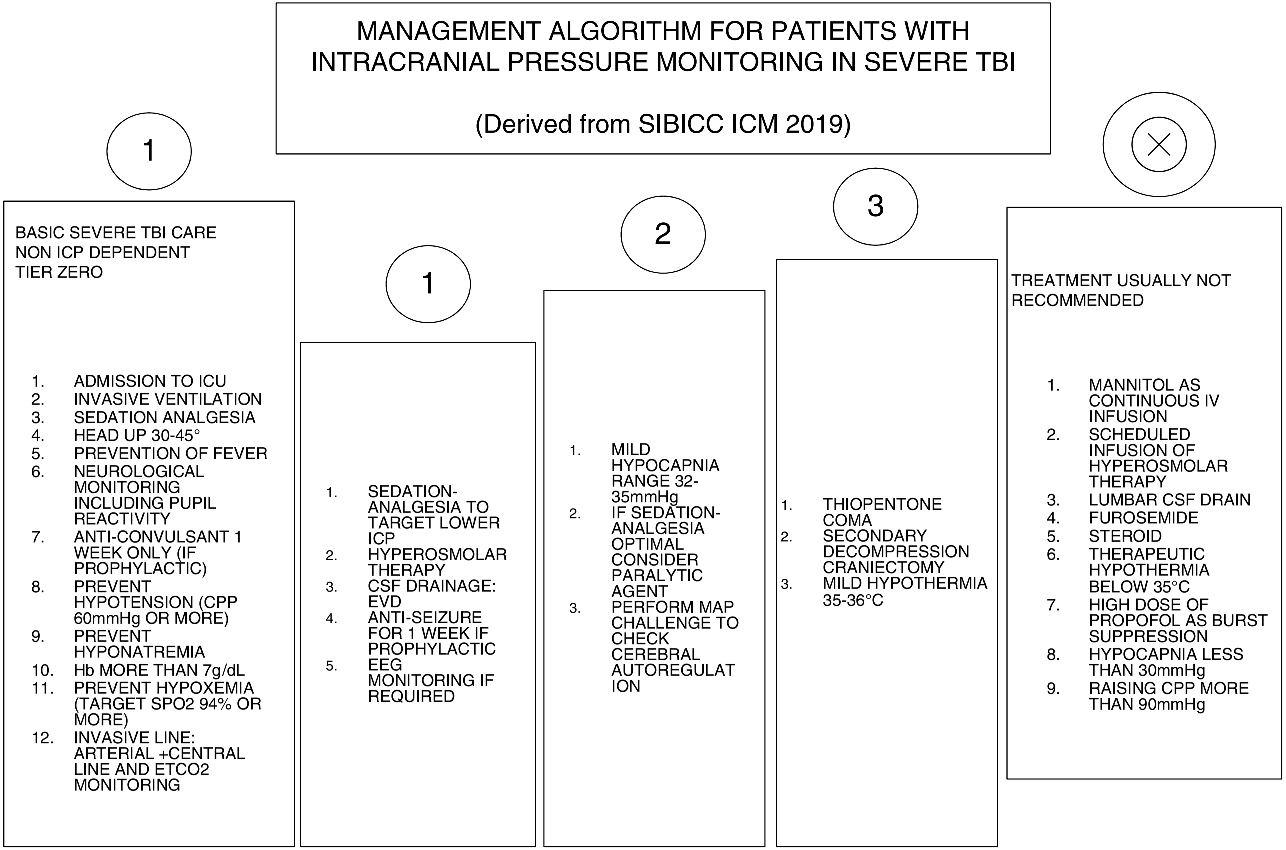
MANAGEMENT ALGORITHM FOR PATIENTS WITH INTRACRANIAL PRESSURE MONITORING IN SEVERE TBI
(Derived from SIBICC ICM 2019)
1
BASIC SEVERE TBI CARE
NON ICP DEPENDENT
TIER ZERO
1. ADMISSION TO ICU
2. INVASIVE VENTILATION
3. SEDATION ANALGESIA
4. HEAD UP 30-45°
5. PREVENTION OF FEVER
6. NEUROLOGICAL MONITORING INCLUDING PUPIL REACTIVITY
7. ANTI-CONVULSANT 1 WEEK ONLY (IF PROPHYLACTIC)
8. PREVENT HYPOTENSION (CPP 60mmHg OR MORE)
9. PREVENT HYPONATREMIA
10. Hb MORE THAN 7g/dL
11. PREVENT HYPOXEMIA (TARGET SPO2 94% OR MORE)
12. INVASIVE LINE: ARTERIAL +CENTRAL LINE AND ETCO2 MONITORING
1
1. SEDATION-ANALGESIA TO TARGET LOWER ICP
2. HYPEROSMOLAR THERAPY
3. CSF DRAINAGE: EVD
4. ANTI-SEIZURE FOR 1 WEEK IF PROPHYLACTIC
5. EEG MONITORING IF REQUIRED
2
1. MILD HYPOCAPNIA RANGE 32-35mmHg
2. IF SEDATION-ANALGESIA OPTIMAL CONSIDER PARALYTIC AGENT
3. PERFORM MAP CHALLENGE TO CHECK CEREBRAL AUTOREGULATION
3
1. THIOPENTONE COMA
2. SECONDARY DECOMPRESSION CRANIECTOMY
3. MILD HYPOTHERMIA 35-36°C
TREATMENT USUALLY NOT RECOMMENDED
1. MANNITOL AS CONTINUOUS IV INFUSION
2. SCHEDULED INFUSION OF HYPEROSMOLAR THERAPY
3. LUMBAR CSF DRAIN
4. FUROSEMIDE
5. STEROID
6. THERAPEUTIC HYPOTHERMIA BELOW 35°C
7. HIGH DOSE OF PROPOFOL AS BURST SUPPRESSION
8. HYPOCAPNIA LESS THAN 30mmHg
9. RAISING CPP MORE THAN 90mmHg

Fig. 14.2 Tier-based approach for ICP management and not to do interventions

Table 14.3 Difference between SDH and EDH, indication of surgery, and different surgical options

Acute extradural hemorrhage	Acute subdural hemorrhage
Middle meningeal artery: source	Bridging cortical veins: source
Limited by sutures	Crossing cranial suture
Commonly associated with fractures	Not associated with fractures
Lucid interval followed by unconsciousness	Gradually increasing headache and confusion
Biconvex shape	Crescent shape
Surgical approach: mostly required	Required based on neurological status (GCS), midline shift and volume
Unilateral	Bilateral/unilateral
Indication of surgery	
Volume of more than 30 mL Thickness of more than 15 mm Midline shift of more than 5 mm or GCS of 8 or less	Thickness of more than 10 mm or Midline shift of more than 5 mm on CT scan Regardless of GCS score
Surgical options	
Craniotomy	Craniotomy (or small sized burr holes) with hematoma evacuation
	Hematoma irrigation with trephination

Step 5: Advance Multimodal Neuromonitoring (Fig. 14.3) Tool to Monitor CPP If Resource Available

- Identification of the range of autoregulation following TBI to provide individualized CPP therapy may be a means to improve outcome and is made possible by newer monitoring devices.
- Jugular venous oxygen saturation ($SjvO_2$): Used to estimate the balance between global cerebral oxygen delivery and uptake. Both reduction in $SjvO_2 < 50\%$ and $SjvO_2 > 75\%$ after TBI are associated with poor outcomes. Monitoring of $SjvO_2$ following TBI may lead to improved outcomes.
- Brain tissue oxygen tension: $PbtO_2$ represents the balance between oxygen delivery and cellular oxygen consumption. $PbtO_2$ provides a highly focal analysis of brain milieu and may be used to monitor the potentially salvageable penumbra following TBI. Normal values are between 35 and 50 mmHg. Following TBI, reduced levels of $PbtO_2$ (<5–10 mmHg) have been seen to be associated with poorer outcomes.
- Cerebral microdialysis: Increasingly used as a bedside tool to provide analysis of brain homeostasis in the intensive care setting. Severe ischemia is usually associated with significant increases in the lactate/pyruvate ratio (>20–25) and is associated with poor outcomes following TBI.
- *Autoregulation:*
  - *MAP challenge:* Record baseline data, that is, ICP, MAP, and CPP. Start vasopressor titrate with MAP elevation by 10 mmHg for 20 min. Record the second set of data. Compare values in autoregulation curve. Disrupted autoregulation characterized by the sustained increase in ICP with MAP elevation. Adjust new MAP based on intact versus disrupted static pressure autoregulation status (sPAR).

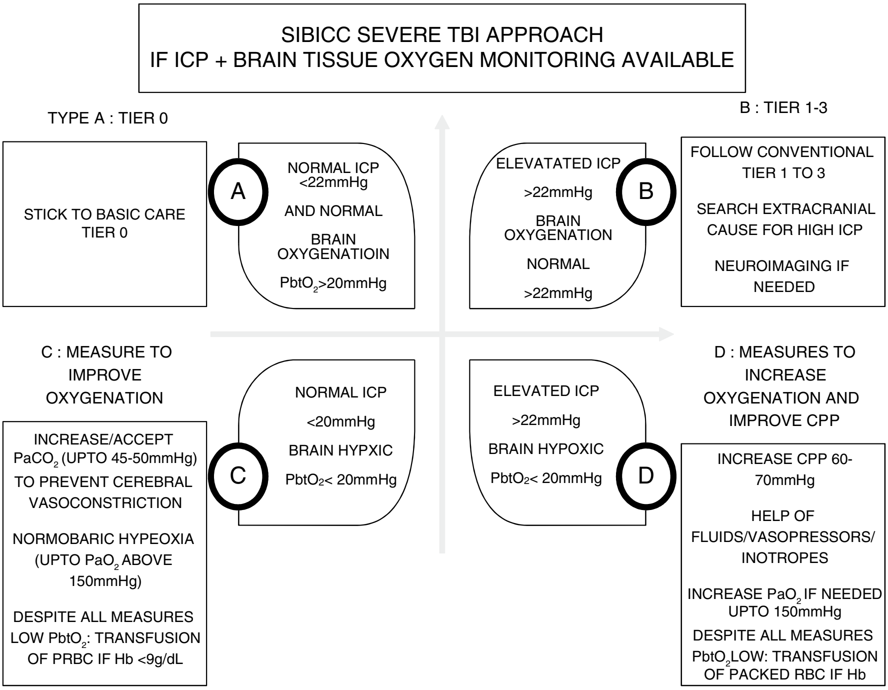
SIBICC SEVERE TBI APPROACH
IF ICP + BRAIN TISSUE OXYGEN MONITORING AVAILABLE
TYPE A : TIER 0
STICK TO BASIC CARE TIER 0
A
NORMAL ICP <22mmHg
AND NORMAL
BRAIN OXYGENATIOIN
PbtO2>20mmHg
B : TIER 1-3
ELEVATATED ICP
>22mmHg
BRAIN OXYGENATION
NORMAL
>22mmHg
B
FOLLOW CONVENTIONAL TIER 1 TO 3
SEARCH EXTRACRANIAL CAUSE FOR HIGH ICP
NEUROIMAGING IF NEEDED
C : MEASURE TO IMPROVE OXYGENATION
INCREASE/ACCEPT PaCO2 (UPTO 45-50mmHg) TO PREVENT CEREBRAL VASOCONSTRICTION
NORMOBARIC HYPEOXIA (UPTO PaO2 ABOVE 150mmHg)
DESPITE ALL MEASURES LOW PbtO2: TRANSFUSION OF PRBC IF Hb <9g/dL
C
NORMAL ICP
<20mmHg
BRAIN HYPXIC
PbtO2< 20mmHg
ELEVATED ICP
>22mmHg
BRAIN HYPOXIC
PbtO2< 20mmHg
D
D : MEASURES TO INCREASE OXYGENATION AND IMPROVE CPP
INCREASE CPP 60-70mmHg
HELP OF FLUIDS/VASOPRESSORS/ INOTROPES
INCREASE PaO2 IF NEEDED UPTO 150mmHg
DESPITE ALL MEASURES PbtO2 LOW: TRANSFUSION OF PACKED RBC IF Hb

Fig. 14.3 Severe TBI algorithm by SIBICC when advanced monitoring tool available

Step 6: Pharmacotherapy

Reversal of Anticoagulation Therapy (Fig. 14.4)

Routine use of platelet transfusion is not recommended in TBI who are on platelet inhibitors.

No evidence that DDAVP (desmopressin) administration in hemorrhagic TBI (under the effect of platelet inhibitors) improves neurological outcome and reduce progression of hematoma. Four-factor PCC recommended in comparison to plasma (FFP) for treating hemorrhagic TBI patients on vitamin-K antagonists (VKAs) (PCCs normalize INR faster than plasma, and evidence suggest that quicker INR reversal reduces hematoma expansion).

- *Tranexamic acid*
  - CRASH-3 trial shows that use of tranexamic acid in TBI is safe and should be used in 3 h of injury leads to favorable outcome, that is, reduces head injury-related death observed.

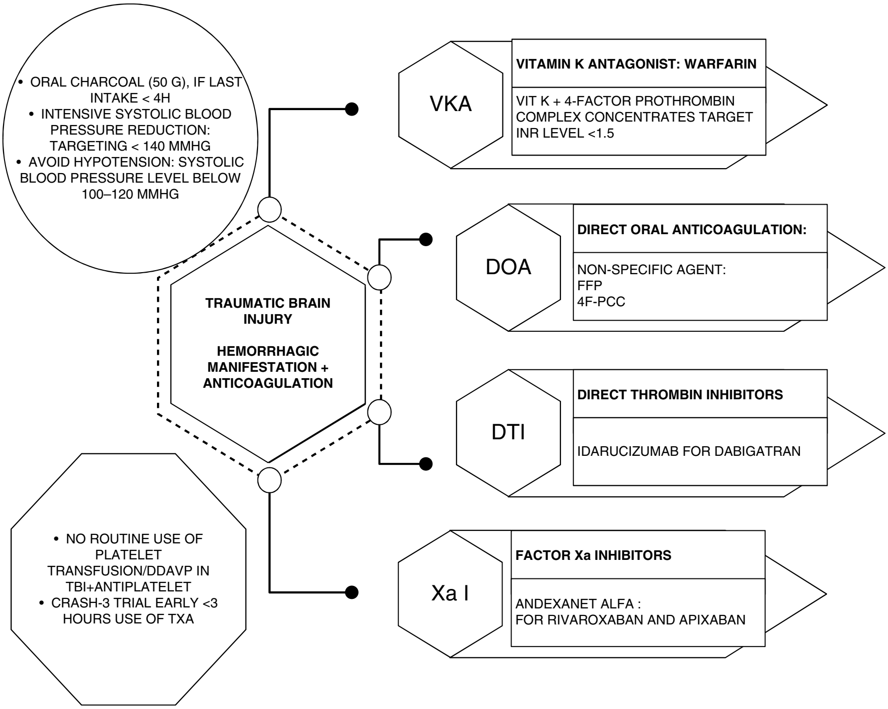
• ORAL CHARCOAL (50 G), IF LAST INTAKE < 4H
• INTENSIVE SYSTOLIC BLOOD PRESSURE REDUCTION: TARGETING < 140 MMHG
• AVOID HYPOTENSION: SYSTOLIC BLOOD PRESSURE LEVEL BELOW 100–120 MMHG
TRAUMATIC BRAIN INJURY
HEMORRHAGIC MANIFESTATION + ANTICOAGULATION
• NO ROUTINE USE OF PLATELET TRANSFUSION/DDAVP IN TBI+ANTIPLATELET
• CRASH-3 TRIAL EARLY <3 HOURS USE OF TXA
VKA
VITAMIN K ANTAGONIST: WARFARIN
VIT K + 4-FACTOR PROTHROMBIN COMPLEX CONCENTRATES TARGET INR LEVEL <1.5
DOA
DIRECT ORAL ANTICOAGULATION:
NON-SPECIFIC AGENT:
FFP
4F-PCC
DTI
DIRECT THROMBIN INHIBITORS
IDARUCIZUMAB FOR DABIGATRAN
Xa I
FACTOR Xa INHIBITORS
ANDEXANET ALFA :
FOR RIVAROXABAN AND APIXABAN

Fig. 14.4 Reversal agent and approach in TBI on anticoagulant therapy

- *Anticonvulsant therapy*
  - Post-traumatic seizures are a major cause of secondary brain injury following TBI and are associated with higher injury severity and worse outcomes. Seizures occur in up to 20% of patients with TBI. These seizures are usually nonconvulsive in nature and cannot be detected clinically and EEG monitoring (preferably continuous) is needed for this.
  - This should be clinically suspected if consciousness impairment is disproportioned to the severity of injury.
  - Phenytoin or levetiracetam (20 mg/kg IV over 60 min followed by 1000 mg IV over 15 min every 12 h) is effective in decreasing the rate of early post-traumatic seizures in the first 7 days of injury, but has no significant role in the prevention of post-traumatic seizures after the first week of injury.
  - Patients with TBI who develop any seizures will require prolonged antiseizure medications.
- *Role of steroids*
  - No benefit in lowering ICP or improvement in patient outcome has been shown using high-dose corticosteroids in acute TBI.
  - The use of methylprednisolone in patients with moderate-to-severe TBI has been demonstrated to increase mortality and is contraindicated (CRASH-1 trial).

Table 14.4 Goals of treatment

Clinical	Systolic BP	≥100 mmHg, avoid hypotension
Laboratory	Temperature	36–38°, avoid hyperthermia
	Hb	≥7gm/dL
	Glucose	140–180 mg/dL
	INR	≤1.4
	pH	7.35–7.45
	$PaCO_2$	35–45, never less than 30 mmHg
	PaO_2	≥80 mmHg, avoid hypoxemia
	Na	135–145
	Platelet	≥80,000
Monitoring	CPP	≥60 mmHg, 60 to 70 mmHg
	ICP	<22 mmHg
	$PbtO_2$	≥20
	SPO_2	≥95%
No role of prophylactic antibiotic. No role of steroid.		

- *Antibiotic therapy*
  - Since TBI patients are more likely to receive invasive monitoring and therapeutic treatments, including mechanical ventilation, they are also more likely to be at increased risk for the development of infections.
  - Sources of potential infections need to be identified and appropriate therapy should be instituted. A common source of infection is invasive monitoring of ICP. The incidence of ICP device infection has been reported to range from 1% to 27%.
  - The current guidelines suggest the use of antibiotic-impregnated EVD catheters to reduce infection rates (weak evidence).
  - Prophylactic antibiotic should be avoided.
- *Role of tracheostomy*
  - Early tracheostomy (preferably percutaneous) should be performed to reduce ventilation days in patients with anticipated prolonged ventilation and /or need for airway protection (particularly for the neurotrauma subgroup).
  - The goals of treatment including clinical, laboratory, and monitoring parameters are summarized in Table 14.4.

Step 7: Supportive Care and ICU Bundle

- *Glycemic control*
  - Prevention of hyper- and hypoglycemia glucose-containing fluids should be avoided and blood sugar monitored to maintain levels between 140 and 180 mg/dL.
- *Nutrition*
  - Early nutritional support is associated with better outcomes and early enteral feeding has been found to be beneficial (within 24–48 h).

  - Indirect calorimetry is the gold standard for the determination of energy requirement (if not basic weight-based equation/predictive equation should be used).
  - Calculated or measured caloric replacement (100–140% of basal expenditure) should be started early and the full goal should be reached by 5–7 days.
  - Post-pyloric feeding may also be used to reduce the risk of ventilator-associated pneumonia.
  - Patients with severe TBI have gastric feeding intolerance. Prokinetic agents, such as metoclopramide, may improve feeding tolerance.
  - Supplemental parenteral nutrition (after 7–10 days) should be considered if unable to achieve 60% of the requirement by enteral route alone.
- *Temperature management*
  - Avoidance and aggressive treatment for fever (core temperature > 38 °C) should be instituted and normothermia should be maintained.
  - Prevention of hyperthermia: In clinical practice, even mild hyperthermia has been associated with poorer outcomes and longer ICU stays as it may lead to increased edema and inflammation.
  - Use of induced hypothermia (32–35 °C) in TBI should be avoided as a signal of harm (Eurotherm3235 trial).
- *Thromboprophylaxis*
  - Ideally pharmacological thromboprophylaxis should be started as soon as possible in TBI cases considering the risk and benefit between hematoma expansion versus VTE risk.
  - But in cases of active bleeding, higher chances of brain hematoma expansion, blunt solid organ injury, and spine injury, this can be delayed 24–72 h. In this phase, mechanical thromboprophylaxis (intermittent pneumatic compression device) use is justified.
  - After imaging stability and conjunction with a neurosurgical consultant, can start pharmacological thromboprophylaxis.
  - Low-molecular-weight heparin (LMWH) is preferred over unfractionated heparin (UFH).
  - Dose of LMWH for DVT prophylaxis in TBI is 30 mg (enoxaparin) subcutaneously 12 hourly (for 50–60 kg) and dose of UFH is 5000 U subcutaneously 8 hourly.
  - If creatinine clearance (CrCl) <30: advisable to choose UFH.
  - Dose of LMWH should be adjusted based on factor Xa level, CrCl, and weight of the patient.
- Stress ulcer prophylaxis (i.e., early enteral nutrition, H_2 blockers, or proton pump inhibitors), physiotherapy, and skin/eye care are also crucial elements of traumatic brain injury patients.

Step 8: Identify Complications of TBI

Complications of TBI

1. Trauma-induced coagulopathy
2. Acute respiratory distress syndrome (ARDS)/negative pressure pulmonary edema
3. Paroxysmal sympathetic hyperactivity/stress cardiomyopathy
4. Hypothalamic-pituitary-adrenal dysfunction/syndrome of inappropriate antidiuretic hormone secretion (SIADH)/cerebral salt wasting/diabetes insipidus (DI)
5. Hydrocephalus
6. Heterotopic ossification
7. Spasticity
8. Chronic traumatic encephalopathy/post-traumatic headache and depression/Cognitive impairment
9. GI and GU complications
10. Gastric ulceration and deep vein thrombosis (DVT)

Step 9: Measure the Outcome after TBI

- Three tools commonly used to measure outcomes after TBI are the Functional Independence Measure (FIM), Glasgow Outcome Scale (GOS), and Disability Rating Scale (DRS).

Step 10: Know the Prognosis

- Very difficult and complex.
- Generally, patients with GCS < 8 have a 30% risk of mortality.
- Patients who remain in a vegetative state or minimally conscious state have a poor chance of meaningful recovery.
- Recovery with functional independence or partial dependence may occur in >50% of severe TBI over a period of years if initial aggressive management is pursued.
- Individual risk factors for poor outcome are low GCS score (especially GCS motor score) increasing age, bilaterally absent pupillary light reflex, associated injuries, abnormal CT scan, hypotension, hypoxemia, elevated ICP, reduced CPP, bleeding diathesis, and pyrexia.
- CT findings associated with poor prognosis: absence or compressed basal cisterns, tSAH (traumatic SAH), presence and degree of midline shift (CT severity) and presence of abnormalities in initial CT.

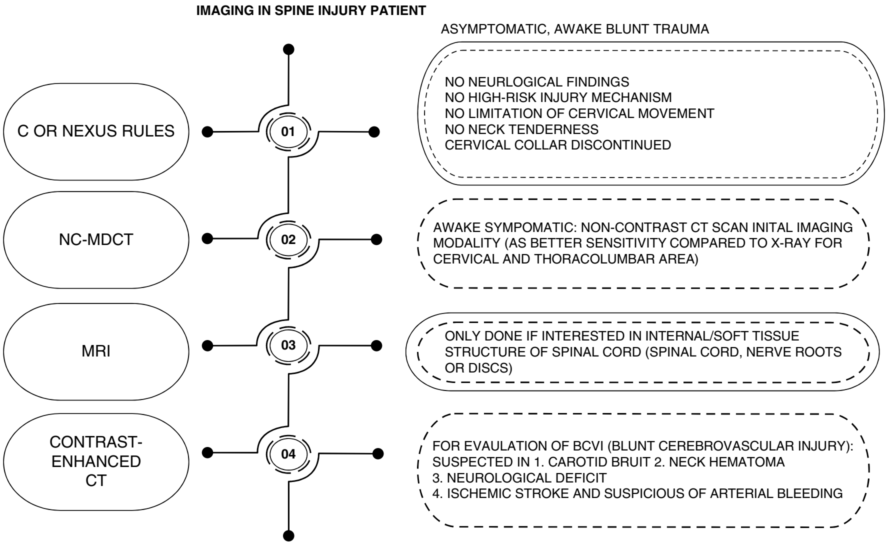
IMAGING IN SPINE INJURY PATIENT
ASYMPTOMATIC, AWAKE BLUNT TRAUMA
C OR NEXUS RULES
01
NO NEURLOGICAL FINDINGS
NO HIGH-RISK INJURY MECHANISM
NO LIMITATION OF CERVICAL MOVEMENT
NO NECK TENDERNESS
CERVICAL COLLAR DISCONTINUED
NC-MDCT
02
AWAKE SYMPOMATIC: NON-CONTRAST CT SCAN INITAL IMAGING MODALITY (AS BETTER SENSITIVITY COMPARED TO X-RAY FOR CERVICAL AND THORACOLUMBAR AREA)
MRI
03
ONLY DONE IF INTERESTED IN INTERNAL/SOFT TISSUE STRUCTURE OF SPINAL CORD (SPINAL CORD, NERVE ROOTS OR DISCS)
CONTRAST-ENHANCED CT
04
FOR EVAULATION OF BCVI (BLUNT CEREBROVASCULAR INJURY): SUSPECTED IN 1. CAROTID BRUIT 2. NECK HEMATOMA
3. NEUROLOGICAL DEFICIT
4. ISCHEMIC STROKE AND SUSPICIOUS OF ARTERIAL BLEEDING

Fig. 14.5 Imaging choices in spine injury patient

Traumatic Spine Injury

- Spine injury, with or without neurological deficits, must always be considered in patients with multiple injuries. Approximately 5% of patients with brain injury have an associated spinal injury, whereas 25% of patients with spinal injury have at least a mild brain injury and injury to limbs and viscera.
- Approximately 55% of spinal injuries occur in the cervical region producing quadriparesis, 15% in the thoracic region, 15% at the thoracolumbar junction, and 15% in the lumbosacral area. Up to 10% of patients with a cervical spine fracture have a second, non-contiguous vertebral column fracture.

Choose an appropriate imaging for assessing spinal injury (Fig. 14.5).

Early management should incorporate a full Advanced Trauma Life Support (ATLS) assessment with the intent to avoid hypotension, bradycardia, and hypoxia.

Manage Traumatic Spinal Injury Patient

1. Early intubation and mechanical ventilation are recommended for patients with high cervical injuries (C1–C5).
2. All trauma victims with suspected cervical spine injury should have cervical spine immobilized until an unstable fracture has been ruled out.
3. All patients with suspected cervical spine injury should have complete spinal imaging by X-ray or CT scan.

4. Urgent neurosurgical consultation.
5. Mean arterial pressure (MAP) augmentation with norepinephrine (if needed) is recommended for at least the first 72 h following injury to a maximum of 7 days. Goal MAP ≥85 mmHg for blunt/incomplete penetrating injury. Goal MAP ≥65 mmHg for complete penetrating injury.
6. Use of high-dose methylprednisolone is not recommended routinely (not after 8 h of onset of injury). Even if it used, it should be within 8 h of onset of injury and in isolated nonpenetrating spinal cord injury as a 30 mg/kg IV bolus followed by an infusion of 5.4 mg/kg/h for 23 h.
7. Early (definition of early not standardized ranging from <8 h to <72 h) neurosurgical decompression of acute spinal cord compression is recommended.
8. Venous thromboembolism prophylaxis should be initiated within first 72 h of injury.
9. Consider early (definition of early not standardized) tracheostomy in high cervical injury (C1–C5) patients.

    Rehabilitation should be offered to all patients.

Continue ICU Bundle Care

Nutrition, bowel care (as patient may develop neurogenic bladder and require urinary catheterization), skin care and bed sore prevention, psychological support, thromboprophylaxis, ulcer prophylaxis, and treatment of spasticity and neuropathic pain are the supportive care required in spine injury patient.

Suggested Reading

A clinical practice guideline for the management of acute spinal cord injury: introduction, rationale, and scope. Global Spine J. 2017; 7(3S):84S–94S. *The ultimate goal of these guidelines is to improve outcomes and reduce morbidity in patients with SCI by promoting standardization of care and encouraging clinicians to make evidence-informed decisions*.

ATLS, Trauma Life Support, Student Course Manual, Tenth edition. *A reference manual on trauma life support for beginners.*

Best practice guideline on spine surgery by American College of Surgeons; 2022.

Congress of neurological surgeons systematic review and evidence-based guidelines on the evaluation and treatment of patients with thoracolumbar spine trauma: executive summary. Neurosurgery. 2019;84:2–6. *A systematic review of the literature was using the National Library of Medicine PubMed database and the Cochrane Library for studies relevant to thoracolumbar spinal injuries based on specific clinically oriented questions. Relevant publications were selected for review.*

Ghaith HS, Nawar AA, Gabra MD, et al. A literature review of traumatic brain injury biomarkers. Mol Neurobiol. 2022;59:4141–58. https://doi.org/10.1007/s12035-022-02822-6.

Guidelines for the management of severe traumatic brain injury, brain trauma foundation, 4th Edition. Neurosurgery. 2017;80(1):6–1. *A comprehensive evidence based guideline on the subject*.

Birrer K, et al. Severe traumatic brain injury management. Surgical Critical Care Evidence-Based Medicine Guidelines Committee; revised 2017. *A comprehensive evidence based guideline*.

Management of traumatic brain injury patients. Korean J Anesthesiol. 2018;71(1): 12–21. *Protocol-based approaches to the management of severe TBI as per recent guidelines.*

Menditto VG, Rossetti G, Sampaolesi M, Buzzo M, Pomponio G. Traumatic brain injury in patients under anticoagulant therapy: review of management in emergency department. J Clin Med. 2024;13:3669. https://doi.org/10.3390/jcm13133669.

SIBICC guideline for severe TBI 2019.

Systemic complications of traumatic brain injury. Curr Opin Anaesthesiol. 2015;28(5):525. *A detailed description of effective management of TBI beyond formulaic-based pursuit of physiological targets and a detailed understanding of the multisystem response of the body.*

Websites

Acute Spinal Cord Injury Management, 2018.
SurgicalCriticalCare.net
www.braintrauma.org

Torso Trauma

15

Prasad Rajhans, Gouri Ranade, Deepak Govil,
and Praveen Kumar

A 30-year-old man was hit by a motor vehicle about 3 h ago. At presentation, he had a threatened airway with labored breathing; his respiratory rate was 32/min with O2 saturation of 85%. He had paradoxical chest movements and decreased air entry on the left side. His heart rate was 120/min, blood pressure was 100/80 mmHg, and Glasgow coma scale (GCS) score was 15/15. After initial stabilization and left-sided intercostal drainage (ICD), the secondary survey revealed abdominal distention with tenderness over the left upper quadrant of the abdomen. A computed tomography (CT) scan of the chest and abdomen showed multiple rib fractures on the left side of the chest with underlying lung contusion and ICD in situ. It also revealed a shattered spleen and 3-cm laceration in segment 6 of the liver along with a 1-cm laceration in the upper pole of the left-sided kidney and pneumoperitoneum, suggesting both solid and hollow viscous injury. An exploratory laparotomy was performed. The liver and kidney were preserved, while the spleen was removed, and primary repair of the bowel segment was performed. The patient gradually recovered in the intensive care unit (ICU).

Multiple life-threatening conditions can result from thoracic and abdominal trauma. Multiple factors, including mechanism of injury, injured body region, hemodynamic status, and associated injuries, determine the diagnostic approaches.

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Step 1: Perform Primary Survey, Resuscitation, and Secondary Survey

Primary Survey (A–E)

A. *Airway with cervical spine protection*: Evaluation of the airway is the first priority during the primary survey. All patients presenting with threatened airways and respiratory distress should have their airways secured.

   Cervical immobilization is maintained until radiological and/or clinical means exclude the injury. Remember the Canadian C-Spine Rule (CCR) and NEXUS Criteria for C-Spine evaluation.

B. *Breathing and ventilation*: Expose the chest to observe chest wall movement, breathing pattern, percuss for dullness/hyperresonance, auscultate breath sounds, and monitor oxygenation. Every polytrauma patient should receive supplementary oxygen till a complete evaluation of all injuries is done.

   - Point-of-care ultrasound: In trauma care, the extended focused assessment with sonography for trauma (E-FAST) is a critical tool during the primary survey. It helps identify pericardial tamponade, hemoperitoneum, and pneumothorax. For trauma patients who are unstable, hypotensive, or pulseless, any abnormal findings on E-FAST should prompt immediate intervention. Diagnostic peritoneal tap is performed only when E FAST is not available.
   - Life-threatening injuries that should be identified and treated during the primary survey are the following:
     - Tension pneumothorax: Immediate large needle decompression should be done in the fifth intercostal space in the midaxillary line or second intercostal space in the midclavicular line or finger thoracostomy, followed by intercostal tube insertion. Positive pressure ventilation after intubation may worsen the tension pneumothorax.
     - Massive hemothorax (more than 1500 ml blood or more than one-third of patient's blood volume in thoracic cavity)—Insert a large-bore (28–32 F) chest tube, replace volume, and get a surgical consult.
     - Open pneumothorax—Flutter valve dressing, taped on three sides, followed by chest tube insertion and surgical closure of the wound.
     - Cardiac tamponade—Pericardiocentesis as a life-saving maneuver followed by immediate thoracotomy or sternotomy.
     - Tracheobronchial disruption—Guided intubation distal to the injury site, or unilateral ventilation and immediate surgical intervention.

C. *Circulation with hemorrhage control*: The pulse rate, blood pressure, and level of consciousness determine the grade of shock. Take two large bore size 14- or 16-gauge iv cannula peripherally. Collect blood for grouping and cross-matching. Circulation volume has to be maintained with isotonic fluids (IV Ringer's Lactate 1 liter stat) and blood and blood product transfusions. Identify the source of bleeding and control it. Look for external bleeding, bleeding in the thorax, abdomen, pelvis, and long bones. Urgent hemostatic laparotomy should be considered in all patients with hemodynamic instability and positive abdominal FAST. External pelvic stabilization with a pelvic binder or a sheet applied at the level of greater trochanter of femur is required in suspected pelvic fractures or unstable pelvis.

D. *Disability (neurological evaluation)*: Assess GCS and evaluate the pupillary size and reaction to light. Low GCS score may be due to decreased cerebral oxygenation or perfusion (shock) or direct cerebral injury. Prevent secondary brain injury by maintaining adequate oxygenation and perfusion.

E. *Exposure/environment control*: Completely undress the patient for thorough examination and assessment. Do not forget to examine the back. A warm environment should be maintained to avoid hypothermia. Use warm fluids and warm blankets to prevent hypothermia. Perineal and vaginal injuries are often missed. One may need to do the log roll to examine the back.

Primary adjuncts—Urinary and gastric catheters, chest X-ray AP and pelvic X-ray AP films, eFAST/DPL, ECG, ABG, and capnography are primary adjuncts during the primary survey.

Secondary Survey

- This involves detailed pertinent history, a complete in-depth physical examination, with reassessment of vital signs. Additional investigations like X-rays, contrast CT, and other diagnostic tests will be required to identify all injuries. The secondary survey also involves tubes and fingers in all orifices. ETT, NG tube, urinary catheter, per rectal examination, and per vaginal examination. Injuries to be identified in the secondary survey include the following:
  - Blunt cardiac injury.
  - Traumatic aortic disruption.
  - Traumatic diaphragmatic injury.
  - Blunt esophageal rupture .
  - Subcutaneous emphysema.
  - Rib, sternum, and scapular fractures.
  - Pelvic fractures.
  - Solid organ and hollow viscus injuries.
  - Genitourinary injuries.
  - In blunt abdominal trauma, pancreatic, mesenteric, and diaphragmatic injuries are less common, difficult to diagnose, recognized late, and potentially dangerous.
  - Look for intra-abdominal injury in all patients with altered sensorium and severe extra-abdominal injuries.
  - Signs and symptoms of abdominal injury are often attenuated in patients >60 years.
  - Pedestrians usually sustain a triad of injuries to leg, torso, and cranium.
  - Look for seatbelt signs, rebound tenderness, abdominal distension, and guarding.
  - Microscopic hematuria in a non-catheterized urine increases the likelihood of intra-abdominal injury.

Step 2: Triage for Surgery

Once the primary survey is concluded, the next step is to triage the nonresponders to emergency surgery—exploratory laparotomy or thoracotomy for damage control or definitive surgery as the clinical situation demands.

- Indications for urgent thoracotomy include
  - ICD output: blood more than 1500 mL immediately following insertion of the drain or more than 200 mL/h for 2–4 h
  - Endobronchial blood loss
  - Massive pulmonary contusion leading to significant impairment of ventilation
  - Significant tracheobronchial tree injury
  - Injury of the heart or great vessels leading to pericardial tamponade and hemorrhagic shock
  - Penetrating chest injury as a cause of hemodynamic instability
- Indications for urgent laparotomy include
  - Hemodynamic instability with penetrating trauma or positive FAST examination in blunt trauma
  - Transperitoneal gunshot injury
  - Clinical signs suggesting peritonitis and evisceration
- The rest of the patients should undergo further necessary radiological investigations to identify and assess the exact anatomical injuries and their severity.
- Guard against exacerbating spinal injuries while positioning patients for imaging.

A simplified approach for the evaluation and management of blunt trauma of the abdomen is discussed in Fig. 15.1.

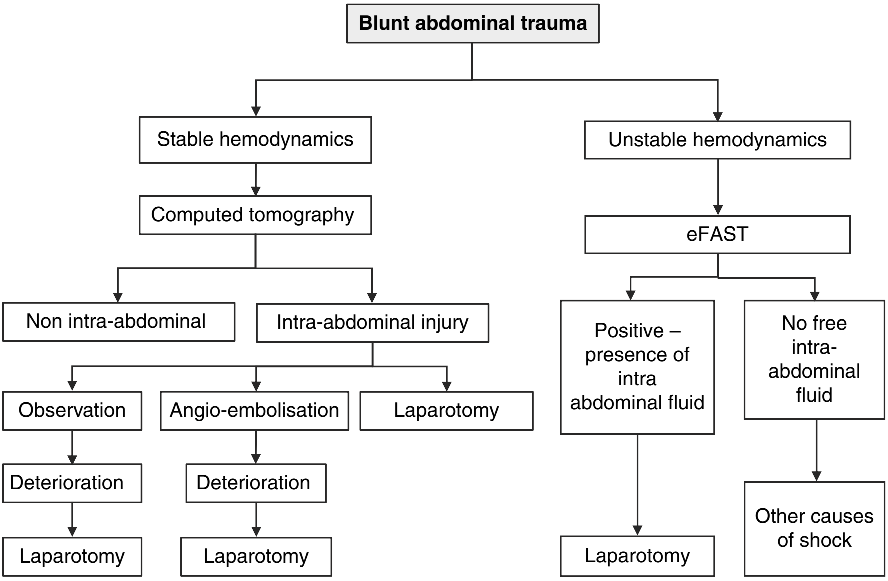
Blunt abdominal trauma
Stable hemodynamics
Unstable hemodynamics
Computed tomography
eFAST
Non intra-abdominal
Intra-abdominal injury
Positive – presence of intra abdominal fluid
No free intra-abdominal fluid
Observation
Angio-embolisation
Laparotomy
Deterioration
Deterioration
Laparotomy
Laparotomy
Laparotomy
Other causes of shock

Fig. 15.1 Simplified approach to the management of abdominal trauma. No intrabdominal injury

Step 3: Triage the Patients to the ICU

- Triaging the patients to the ICU or the floor (wards) is decided of based on the severity of the injury and the extent of surgery, requirement for the mechanical ventilation and inotropic support, age, and comorbidities of the patient.

Step 4: Continue to Observe and Treat

While the need for complete and repeated clinical and eFAST examination in the ICU cannot be overemphasized, the following features will have to be focused during the daily examination of the patients:

A. *Ventilation and circulation assessment*
   - Lung protective ventilator strategies should be applied in all trauma patients, particularly with lung contusions.
   - Pulse rate, blood pressure, urine output, hematocrit, and lactate levels indicate the degree of perfusion and the grade of volume deficit.
   - Unstable or critically ill patients might warrant other invasive monitoring techniques such as intra-arterial pressure and cardiac output measurements. Echocardiography should be performed repeatedly for the assessment of circulation.
   - Circulation is maintained with fluid and blood transfusion with or without inotropic support.

B. *Management of the ICD tube*
   - Monitor the volume and nature of the output daily, column movement, presence of air leak, and lung expansion clinically and radiologically.

   1. Volume
      - Common causes for persistent high output:
        - Ongoing hemorrhage
        - Thoracic duct injury
        - Hypoproteinemia
      - Sudden decrease in the volume of the output: Check for tube blockage or malpositioning. The tube should then be declotted (milking) or repositioned or changed to maintain its patency of the tube.
      - Local thrombolytic agents may be used in exceptional cases to maintain tube patency.
   2. Nature of the output
      - Sanguineous output—ongoing hemorrhage: Output of more than 200 mL/h of sanguineous fluid continuously for 4 h is an indication for thoracotomy.
      - Turbid output with pyrexia—infective focus. Fluid should be sent for further microbiological analysis, and treatment should be started accordingly. Bacterial or fungal growth from a drain that is >24 h old may reflect colonization, a fresh sample with needle aspiration or sample from a new drain should be sent for culture.

- Milky white, high-volume output—thoracic duct injury (chylothorax). Presence of chyle may be confirmed at the bedside by dissolving the drained fluid in equal amount of ether. If it gets dissolved, then it is chyle; otherwise, it is pus. Check the triglyceride level. Low output (<1000 mL/24 h) can be managed conservatively. High output usually requires surgical management.

3. Wide swinging of column movement (>5 cm) is suspicious of poor lung expansion or lung collapse and should be investigated further with the chest X-ray and bronchoscopy if needed.
4. Air leaks indicate the presence of tracheobronchial/parenchymal communication with the pleural cavity.
   - Chest tube insertion sites should be checked for peritubal air entry due to loose sutures.
   - Treatment of air leak: Minor air leaks usually heal with deep breathing exercises. Persistent air leaks, not settling down with chest physiotherapy alone, require application of negative pressure suction (usually 10 cm H_2O) to the underwater seal bottle. Massive air leaks causing oxygen desaturation will require insertion of a second ICD tube and usually thoracotomy.
   - After stoppage of air leak, check the chest X-ray after clamping the tube for 24 h to look for lung collapse, and the ICD tube can be removed if the chest X-ray is normal.
   - In case of subcutaneous emphysema, the extent should be marked and monitored daily for change in extent after insertion of the ICD tube. There is no role for skin incisions.
5. In cases of clotted hemothorax, declotting is done with streptokinase. 1–1.5 million units of streptokinase is diluted in 100 mL and infused through the ICD tube under aseptic precautions. The tube is then clamped for 3–4 h; chest physiotherapy is done and then the tube is opened. This may be repeated once a day for 3–4 days till clots are evacuated. This procedure is not indicated in patients with coagulopathy or patients on systemic anticoagulation therapy like warfarin.
6. Fever, productive cough, and infiltrates in the chest X-ray indicate pulmonary infections. Broad-spectrum antibiotics should be started empirically and changed to specific antibiotics depending on the sensitivity pattern.
7. Radiological investigations
   - Chest X-rays should be done to monitor the lung expansion and after the removal of the ICD tube to look for pneumothorax.
   - Ultrasonography and CT scans should be done for suspected loculated effusions and pneumothorax and to guide its drainage percutaneously.
   - The following conditions should be fulfilled before the removal of the ICD tube:
     - Less than 50–100 mL output and serous in nature

   - Less than 5 cm swinging of air column with normal breathing
   - Full lung expansion
8. Chest tube insertion sites must be inspected every day for infections and air or fluid leakage with regular care of the wound site.

C. *Tracheostomy site and surgical wound sites:* Inspect for surgical site infection.

D. *Regular active and passive chest physiotherapy.* This is required to prevent atelectasis and pneumonia.

E. *Pain control*

Control pain through nonsteroidal anti-inflammatory drugs, opioids, epidural analgesia, and patient-controlled analgesia devices.

F. *Nutrition*

Nutrition is maintained with enteral nutrition in most of the cases.

Abdominal Injuries

Solid organ injuries are managed either nonoperatively or operatively depending on the severity of the injury and the hemodynamic stability of the patient. Hollow viscous injuries are usually managed operatively.

Whenever applicable damage control surgery along with hemostatic resuscitation should be considered as a first-line strategy to prevent triad of death.

Step 5: Nonoperative Management of Solid Organs (Spleen, Liver, and Kidney)

- Nonoperative management should be practiced only in highly specialized trauma centers that have 24-h availability of trauma surgeons and interventional radiologists.
- Initial clinical examination and hemodynamic status dictate the decision rather than the grade of solid organ injury or the degree of hemoperitoneum.
- Daily clinical examination of the abdomen with hemodynamic status assessment based on pulse rate, blood pressure, urine output, abdominal girth, intra-abdominal pressure, and fall in hemoglobin and hematocrit levels.
- No antibiotic coverage is needed in cases of nonoperative management of solid organ injury alone.
- Ultrasound examination of the abdomen is done; if the clinical situation demands, to look for significant increase in the intra-abdominal collection.
- Abdominal distention, development of peritoneal signs, and decrease in urine output indicate ongoing hemorrhage and need for operative management.
- Progressive drop in hematocrit with hemodynamic instability should also indicate the consideration for operative management.
- In case of liver injuries, biliary peritonitis may present the clinical picture of intestinal perforations. Clinical and radiological examinations should be

performed to rule out missed intestinal injuries, and in their absence, percutaneous drainage of the bile collection can be done, avoiding laparotomy.

Step 6: ICU Care After Operative Management of Abdominal Injuries

- Repeated complete physical examinations should be performed every day.
- In case the abdominal closure seems to be difficult during the primary surgery (due to bowel edema/retroperitoneal collection, etc.), it is prudent to leave it open as forceful closure would lead to increase in intra-abdominal pressure resulting in the abdominal compartment syndrome.
- Enteral nutrition is started at the earliest and gradually advanced to regular diet as tolerated.
- Immediate enteral feeding is beneficial (in comparison to parenteral) in a critically ill patient regardless of the patient's premorbid nutritional status.
- Care of the feeding jejunostomy tube should be taken properly.
- Conditions suggesting the need for partial or total parenteral nutrition are as follows:
  - Oral intake less than 50% of the energy needs
  - Unable to tolerate nasogastric or nasojejunal feed for more than 7 days in previously well-nourished patient
  - Nonfunctioning gastrointestinal tract
- Inspection of the surgical sites is done for signs of inflammation and infection.
- Monitoring of the drain output and nature of fluid should be done.
- In case the drains show persistent and or purulent output, it can be indicative of deep surgical site infections or intestinal fistulae. If such is the case, rapid clinical/radiological examination followed by the opening of the laparotomy incision site and thorough lavage is indicated. If intestinal fistulae are present, it should be treated either surgically or nonoperatively depending on its location and output.
- Persistent high drain output in cases of pancreatic and splenic injury should raise suspicion of the pancreatic fistula.
- Drain amylase should be requested on or after the third postoperative day in cases of suspected pancreatic fistula and in cases of pancreatic and splenic injury.
- Continuing with the drains, if necessary CT-guided drainage, antibiotic coverage (if signs of infections present), serial radiological examinations, and drainage of collections are recommended for the treatment of pancreatic fistulae. Use of somatostatin or its analog may be useful in such situations.

Suggested Reading

American College of Surgeons Committee on Trauma. Thoracic trauma, Abdominal and Pelvic trauma. Advanced trauma life support program for doctors. 10th ed. *Comprehensive text in context with advanced trauma life support (ATLS) program.*

Harriss DR, Graham TR. Management of intercostal drains. Br J Hosp Med. 1991;45:383–6. *This report outlines the correct procedure for managing intercostal drains and describes the complications that may occur*.

Ludwig C, Koryllos A. Management of chest trauma. J Thorac Dis. 2017;9(Suppl 3):S172–7. *Detailed review on management of thoracic trauma.*

Miller KS, Sahn SA. Chest tubes. Indications, technique, management and complications. Chest. 1987;91:258–64.

Spahn DR, Bouillon B, et al. The European guideline on management of major bleeding and coagulopathy following trauma: fifth edition. Crit Care. 2019;23(1):9. *Comprehensive guidelines for management of bleeding in a trauma patient.*

16

Burn and Inhalation Injury Management

Sushma Sagar, Shivangi Saha, and Maneesh Singhal

Case Vignette

A 50-year-old man presented to the emergency department (ED) with an alleged history of burns sustained while sleeping in a closed room. On arrival, the primary survey was unremarkable except for a low BP of 80/50 mmHg and hoarseness of voice with the production of sooty sputum. The secondary survey revealed cold, clammy extremities with 60% burns involving the face, torso, and extremities. Over the right lower limb, there were circumferential burns and swelling with absent pulsations. The chest radiograph was normal, and other associated injuries were noted.

The mortality and morbidity of burn patients have improved due to improvements in care over the past few decades. Local burn wound care and long-term systemic, nutritional, and rehabilitative care need to be addressed from the very beginning by the treating team. The care of the burn patient requires very advanced critical care, preferably in a dedicated burn unit.

First Day

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Step 1: Initial Assessment and Resuscitation

All burn patients should be approached as polytrauma patients. All severe burn injuries complicated by major trauma or inhalational injury, chemical burns, high-voltage electrical burns, and in adults deep burns covering more than 20% of body surface area excluding superficial burns should be managed in a dedicated burn unit.

(i) Airway with cervical spine immobilization
  - The initial management of acute burns necessitates airway and cervical spine assessment and stabilization.
  - All patients should immediately receive 100% oxygen supplementation, recognizing that pulse oximetry readings may be falsely reassuring in the setting of carbon monoxide poisoning.
  - A thorough evaluation for signs of inhalational injury is crucial as it significantly impacts morbidity and mortality.
  - Wheezing, tachypnoea, stridor, and hoarseness indicate impending airway obstruction due to an inhalation injury or edema, and immediate treatment is required.
  - If the patient is not breathing or has labored respiration or signs of obstruction, clear the airway by oral/nasal suction followed by orotracheal intubation with inline stabilization of the neck if an injury to the cervical spine is a consideration.
  - Risk of upper airway obstruction increases with the following:
  1. Inhalation burns—carbonaceous sputum, singed nasal hairs
  2. All patients with deep burns of more than 35–40% total burn surface area (TBSA)
  3. Burns involving the face, neck, and upper torso
     – If respiratory failure is imminent, intubation is instituted early, and frequent chest physiotherapy and suctioning are performed to maintain pulmonary hygiene.
     – Early intubation is also performed if the patient requires prolonged transport. Properly securing the airway is of utmost importance to the patient.
  - Airway edema can progress rapidly within the first 24–48 h following a burn, potentially leading to sudden and complete airway obstruction.
  - Pediatric patients, in particular, may tire quickly, and supra-sternal retraction is a clear sign of impending respiratory failure requiring immediate intubation.
  - Once a patient is intubated for inhalational injury, close monitoring is paramount, and extubation should generally be deferred for 48–72 h.
  - The medical management of inhalational injuries often involves a multimodal approach. Nebulized heparin (typically 10,000 IU every 4–6 h for 7 days) and nebulized N-acetylcysteine have been shown to improve airway patency and mitigate the risk of airway complications.

  - Bronchodilator therapy can aid in mucociliary clearance by dilating the airways, while corticosteroids can help reduce airway inflammation.
  - Diagnosis of Inhalational injury is often established by the use of bronchoscopy, which reveals early inflammatory changes such as erythema, edema, ulceration, sloughing of mucosa, and prominent vasculature in addition to infraglottic soot. Management of inhalation injury is directed at maintaining open airways and maximizing gas exchange.
  - A patient who can cough with a patent airway can clear secretions very effectively, and all efforts should be made to treat the patient without mechanical ventilation.
  - Frequent bronchoscopies may be needed to clear inspissated secretions in intubated patients.
  - These patients should be ventilated as per the ARDSnet protocol with low tidal volume (6 mL/kg ideal body weight). Try to keep the plateau pressure below 30 cm H_2O. Deep circumferential chest burn may limit chest wall motility, so a higher plateau pressure up to 40 cm H_2O may be tolerated.

(ii) Carbon monoxide poisoning
  - Beyond airway management, addressing potential complications like carbon monoxide and cyanide poisoning is essential.
  - Carbon monoxide poisoning, diagnosed by elevated carboxyhemoglobin levels on arterial blood gas analysis, requires prompt treatment with 100% oxygen or hyperbaric oxygen therapy to expedite the elimination of carbon monoxide from the body.

(iii) Cyanide toxicity
  - Cyanide toxicity, another potential threat, should be suspected in burn patients presenting with depressed consciousness, lactic acidosis, and a compensatory decrease in EtCO2 on arterial blood gas. Monitoring serum lactate levels and EtCO2 can provide valuable insights into cyanide poisoning.
  - Treatment involves a three-pronged approach: Binding cyanide, inducing methemoglobinemia, and administering sulfur donors. A combination of sodium thiosulfate and hydroxocobalamin has proven effective in treating severe cases. In situations where hydroxocobalamin is unavailable, the Cyanide Antidote Kit, containing amyl nitrite and sodium nitrite for methemoglobinemia induction and sodium thiosulfate as a sulfur donor, can be utilized.

Breathing and Ventilation

- Always be vigilant for acute respiratory distress in burn patients, which may indicate potentially life-threatening conditions like tension pneumothorax, open pneumothorax, or massive hemothorax. These conditions necessitate immediate decompression.

- Additionally, deep circumferential eschar on the chest can restrict breathing and may require urgent escharotomy, which consists of longitudinal incisions in the mid-axillary line and extended for the length of eschar.

Circulation

- Obtain IV access anywhere possible and start giving fluids:
  - Unburned areas are preferred.
  - Burned areas are acceptable.
  - Central access is obtained if expertise is available.
  - Intraosseous route is an alternative in the pediatric age group and is nowadays being used in adults as well.
  - Venous cutdown performed if IV canulation is difficult.
- Perform resuscitation in burn shock (first 24 h):
- Before evaluating the burn size, it is reasonable to initiate intravenous fluids (preferably Ringer's lactate) at a rate of 10 ml/kg/h.
- Once the burn area has been assessed, a more precise calculation of fluid resuscitation volume is necessary. While formulas like the Parkland and modified Brooke were historically popular, current guidelines from the American Burn Association suggest a simplified approach.
- Calculate the initial 24 h resuscitation volume as 2 ml/kg/% TBSA for adults and 3 ml/kg/% TBSA for children under 14 years old, where %TBSA represents the percentage of total body surface area burned. For children weighing less than 30 kg, a 5% dextrose solution in Ringer's lactate at standard maintenance rates is also recommended.
- These formulas provide a starting point, and fluid administration should be tailored to each patient's individual needs. The initial 8 h should focus on delivering half of the calculated fluid volume, with the remaining half administered over the subsequent 16 h.
- Urine output serves as a real-time indicator of fluid resuscitation adequacy. The goal is to maintain a urine output of 0.5–1 ml/kg/h in adults and 1–1.5 ml/kg/h in children by adjusting the fluid administration rate accordingly.
- For patients with extensive burns, urinary catheterization is necessary to allow for continuous monitoring of urine output and ensure appropriate fluid management.
- Large amounts of resuscitative fluids may not be well tolerated and can contribute to the development of ileus, abdominal or extremity compartment syndrome, pulmonary edema, ARDS, and generalized edema.
- These patients should be examined frequently for neurovascular checks to determine the need for escharotomy.

Resuscitation Endpoint

When the maintenance rate is reached (approximately 24 h), change fluids to D5/NS with 20 mEq KCl at the maintenance level:

- Maintenance fluid rate = basal requirements + evaporative losses

- Basal fluid rate
  - Adult basal fluid rate = 1500 mL × body surface area (BSA) (for 24 h)
  - Pediatric basal fluid rate (<20 kg) = 2000 mL × BSA (for 24 h)
- Evaporative fluid loss
  - Adult evaporative fluid loss (mL/h) = (25 + percent TBSA burn) × BSA
  - Pediatric evaporative fluid loss (<20 kg) (mL/h) = (35 + percent TBSA burn) × BSA

Role of Albumin

- For patients in the initial 24 h of burn resuscitation, particularly those with extensive burns, healthcare providers should consider incorporating albumin administration to enhance urine output and potentially decrease the overall volume of fluids required. This recommendation is particularly relevant in situations where a patient's condition is deteriorating despite receiving increasing amounts of crystalloids.

Role of Blood Transfusion

- Hemoconcentration occurs during the first several hours immediately following a severe burn and transfusions are generally unnecessary.

Step 2: Take a Detailed History

- Allergy
- Medication
- Pregnancy/past illness
- Last meal taken
- Environment (associated injuries)

Step 3: Start Supportive Treatment

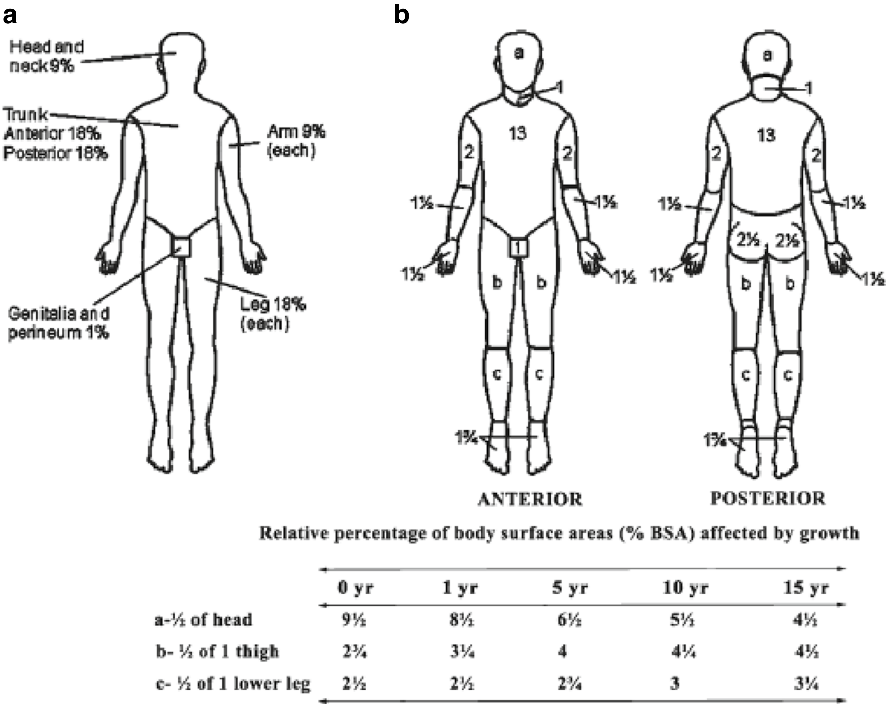
- Initiate early enteral nutrition
- Analgesia, sedation, and delirium management
- Give stress ulcer prophylaxis
- Glycemic control
- Tetanus prophylaxis
- Deep vein thrombosis prophylaxis should be started

Step 4: Assess Severity

- In adults, rule of "nines" is used as a rough indicator of percent TBSA (Table 16.1 and Fig. 16.1).

Table 16.1 Rule of nines for establishing the extent of burned body surface

Anatomic surface	Total body surface (%)
Head and neck	9
Anterior trunk	18
Posterior trunk	18
Arms, including hands	9% each
Legs, including feet	18% each
Genitalia	1


a
Head and neck 9%
Trunk
Anterior 18%
Posterior 18%
Arm 9% (each)
Genitalia and perineum 1%
Leg 18% (each)
b
a
1
13
2
2
1½
1½
1½
1½
1
b
b
c
c
1¾
ANTERIOR
a
1
13
2
2
1½
1½
2½
2½
1½
1½
b
b
c
c
1¾
POSTERIOR

Relative percentage of body surface areas (% BSA) affected by growth

	0 yr	1 yr	5 yr	10 yr	15 yr
a-½ of head	9½	8½	6½	5½	4½
b- ½ of 1 thigh	2¾	3¼	4	4¼	4½
c- ½ of 1 lower leg	2½	2½	2¾	3	3¼

Fig. 16.1 (**a**) Rule of "nines" and (**b**) Lund–Browder diagram for estimating the extent of burns. (Adapted from Artz CP, Moncrief JA. The treatment of burns. 2nd ed. Philadelphia: WB Saunders Company; 1969)

- In children, adjust percent because they have proportionally larger heads (up to 20%) and smaller legs (13% in infants) than adults.
- Lund–Browder diagrams improve the accuracy of the percent TBSA for children.

Depth of Burn Injury

- First-degree burns
  - Damage above the basal layer of the epidermis
  - Dry, red, painful ("sunburn")

- Second-degree superficial burns
  - Damage into dermis
  - Skin adnexa (hair follicles, oil glands, etc.) remain intact
  - Heal by re-epithelialization from skin adnexa
  - The deeper the second-degree burn, the slower the healing (fewer adnexa for re-epithelialization)
  - Moist, red, blanching, blisters, extremely painful
  - Superficial burns heal by re-epithelialization and usually do not scar if healed within 2 weeks
- Second-degree deep burns (deep partial thickness)
  - Damage to deeper dermis
  - Less moist, less blanching, less pain
  - Heal by scar deposition, contraction, and limited epithelialization
- Third-degree burns (full thickness)
  - Entire thickness of skin destroyed (into fat)
  - Any color (white, black, red, brown), dry, less painful (dermal plexus of nerves destroyed)
  - Heal by contraction and scar deposition (no epithelium left in the middle of the wound)
- Fourth-degree burns
  - Burn into muscle, tendon, and bone
  - Need specialized care
  - Deep burns usually need skin grafts to optimize results and lead to hypertrophic (raised) scars if not grafted

Step 5: Burn Wound Care and Control of Infection

- Effective burn wound management aims at maintaining wound cleanliness, promoting the removal of debris and exudate, preventing microbial growth and infection, protecting viable epithelium, fostering tissue regeneration, creating an environment conducive to healing, minimizing pain, and preventing complications like joint stiffness and contractures.
- Partial-thickness burns typically heal within approximately 3 weeks with conservative management, including dressings and topical antimicrobials. Conversely, full-thickness burns necessitate surgical intervention for healing. Burns that cannot be immediately classified as partial or full-thickness require reevaluation within 10–14 days to determine the appropriate surgical approach.
- Treatment for partial-thickness burns often involves cleansing and dressing changes to support epithelialization. While antimicrobial therapy might not be necessary for superficial burns, extensive full-thickness burns often benefit from topical antimicrobials to prevent colonization and maintain moisture. Full-thickness burns, especially those that are circumferential, can restrict skin elasticity and, in conjunction with edema, lead to compartment syndrome, requiring an escharotomy to relieve pressure. Definitive treatment for full-thickness burns

usually involves eschar excision and coverage with skin grafts or flaps. However, temporary dressings, including allografts, xenografts, and biologic dressings, are frequently employed, particularly when immediate grafting is not feasible. These temporary coverings provide a barrier against infection, support re-epithelialization, and allow time for wound healing in this immunocompromised patient population.

Step 6: Supportive Treatment—Nutrition

- Providing early nutritional support is crucial for critically burned patients. Ideally, enteral nutrition should begin within the first 6–12 h after injury to counteract hypercatabolism, prevent stress ulcers, minimize infection risk by reducing bacterial translocation from the gut, and enhance immunoglobulin production.
- The caloric needs are estimated based on the Curreri formula (Table 16.2). Protein needs are approximately 2.5 g/kg.
- Additionally, supplementing micronutrients like zinc, copper, selenium, calcium, and vitamins B1, C, D, and E for up to 1 month post-injury can promote wound healing.

The pediatric formulas have been derived from retrospective analyses of dietary intake, which is associated with the maintenance of average body weight over hospital stay (Table 16.3).

Table 16.2 Curreri formula for estimating caloric requirements for adult burn patients

Age	Formulas
6–60 years	25 kcal/kg/day +40 kcal/percent burn/day
>60 years	25 kcal/kg/day +65 kcal/percent burn/day

Table 16.3 Formulas for estimating the caloric requirements for pediatric burn patients

Age	Formulas
0–1 year	2100 kcal/m^2 TBSA/day +1000 kcal/m^2 TBSA burn/day
1–11 years	1800 kcal/m^2 TBSA/day +1300 kcal/m^2 TBSA burn/day
12–18 years	1500 kcal/m^2 TBSA/day +1500 kcal/m^2 TBSA burn/day

Shriners Hospitals for Children at Galveston, Texas

Step 7: Manage Complications

Successful management of burns involves the management of predicted complications like sepsis, ARDS, and acute kidney injury.

Step 8: Physiotherapy and Psychological Support

Physiotherapy and psychological assessment and care should start from the very beginning and can be continued till the patient gets discharged. Early rehabilitation protocol as per the care facility should be in place for a better outcome.

Suggested Reading

Bacomo FK, Chung KK. A primer on burn resuscitation. J Emerg Trauma Shock. 2011;4:109. *Over-resuscitation, otherwise known as "fluid creep," has emerged as one of the most important problems during the initial phases of burn care over the past decade. To avoid the complications of over-resuscitation, careful hourly titration of fluid rates based on a compilation of various clinical endpoints by a bedside provider is vital. The aim of this review is to provide a practical approach to the resuscitation of severely burned patients.*

Barajas-Nava LA, López-Alcalde J, Roqué i Figuls M, et al. Antibiotic prophylaxis for preventing burn wound infection. Cochrane Database Syst Rev. 2013;CD008738. *The largest volume of evidence suggests that topical silver sulfadiazine is associated with a significant increase in rates of burn wound infection and increased length of hospital stay compared with dressings or skin substitutes; this evidence is at an unclear or high risk of bias. Currently, the effects of other forms of antibiotic prophylaxis on burn wound infection are unclear. One small study reported a reduction in the incidence of pneumonia associated with a specific systematic antibiotic regimen.*

Glas GJ, Levi M, Schultz MJ. Coagulopathy and its management in patients with severe burns. J Thromb Haemost. 2016;14(5):865–74. *A review article on suggested targeted treatments that could benefit patients with severe burns include systemic treatment with anticoagulants.*

Gueugniaud PY, Carsin H, Bertin-Maghit M, Petit P. Current advances in the initial management of major thermal burns. Intensive Care Med. 2000;26:848. *A review article on the management of burn.*

Perel P, Roberts I. Colloids versus crystalloids for fluid resuscitation in critically ill patients. Cochrane Database Syst Rev. 2013;(2). *There is no evidence from randomized controlled trials that resuscitation with colloids reduces the risk of death, compared to resuscitation with crystalloids, in patients with trauma, burns, or following surgery. Furthermore, the use of hydroxyethyl starch might increase mortality. As colloids are not associated with an improvement in survival and are considerably more expensive than crystalloids, it is hard to see how their continued use in clinical practice can be justified.*

Satahoo SS, Parikh PP. Are burn patients really at risk for thrombotic events? J Burn Care Res. 2015;36(1):100–4. *This study seeks to estimate the true rate of DVT in burn patients and evaluate possible risk factors to its development.*

Toon MH, Maybauer MO, Greenwood JE, et al. Management of acute smoke inhalation injury. Crit Care Resusc. 2010;12:53. *A review on the effects of pulmonary injury from smoke inhalation, which is common in burn victims, significantly contributing to the morbidity and mortality of fire-related injuries.*

Wise R, Jacobs J. Incidence and prognosis of intra-abdominal hypertension and abdominal compartment syndrome in severely burned patients: pilot study and review of the literature. Anaesthesiol Intensive Ther. 2016;48(2):95–109. *A review of IAH associated with burn injury. IAH and ACS have a relatively high incidence in burn patients compared to other groups of critically ill patients. The percentage of TBSA burned correlates with the mean IAP. The combination of positive (daily and cumulative) fluid balance, high IAP, high EVLWI, and low APP suggests a poor outcome. Nonsurgical interventions appear to improve end-organ function. Nonresolution of IAH is related to a worse outcome.*

Part IV

Toxicology, Envenomation and Thermo Dysregulation

General Poisoning Management

17

Omender Singh, Prashant Nasa, and Deven Juneja

Case Vignette

A 24-year-old woman was admitted to the hospital with a history of consumption of some liquid at home followed by vomiting, altered mental status, and labored breathing. She was brought to the triage in the comatose state with pinpoint pupils, frothy secretions from her mouth, heart rate 58/min, and blood pressure 90/48 mmHg.

A high index of suspicion for intoxication is warranted in the practice of critical care medicine, particularly for patients admitted with unexplained altered mental status, seizures, cardiac dysrhythmias, and respiratory depression. Diagnosis may be complicated by the possibility of multiple-drug ingestion. Supportive care during the first few hours of admission may be life-saving. Antidotes should be used early on suspicion of a particular poison to prevent organ dysfunction. Attempts to identify the toxin should be done by focused history, a directed physical examination, and commonly available laboratory tests.

Step 1: Initiate Resuscitation and Assessment

- Initiate resuscitation using the ABCDE approach.

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https://doi.org/10.1007/978-981-96-5636-3_17

Airway

- Management of airways is very important in poisoning. Some toxins (acid or alkali ingestion) require extra care during airway management. When intubation is necessary, rapid sequence induction is indicated using short-acting paralytic agents.
- Do not solely use a Glasgow coma scale of <8 to identify the need for intubation in a poisoned patient who is otherwise protecting the airways as many of them may improve over a short time.
- Urine toxicology screening should be obtained before any sedatives or hypnotics are administered.

Breathing

- A patient's oxygenation status can be monitored with a bedside pulse oximeter except for toxins leading to dyshemoglobenemias, that is, in carbon monoxide poisoning, the pulse oximeter is unreliable in detecting carboxyhemoglobin. Similarly, in methemoglobinemia due to cyanide poisoning pulse oximetry saturation is not reliable. In these cases, true oxygen saturation can be measured by coximeter-enabled blood gas analyzer.
- Some newer-generation pulse oximeters are capable of estimating carboxy and methemoglobin continuously by adding additional light-emitting diodes of different wavelengths.
- Give oxygen by the nasal cannula or face mask to maintain SpO_2 of more than 95%. Exceptions include paraquat poisoning, where oxygen therapy should be avoided as it may lead to increased pulmonary injury.
- When the patient is in respiratory distress and not able to maintain oxygenation or ventilation, assisted ventilation should be considered.

Circulation

- Monitor pulse and blood pressure. Do an ECG. Obtain a good peripheral line and start intravenous fluids.

The "coma cocktail" of dextrose (1 Amp D50W IV), naloxone (2 mg IV), flumazenil (0.2 mg IV), and thiamine (100 mg IV) can be considered in unknown poisoning with unconsciousness and coma but should be avoided in patients with a history of benzodiazepines or opiates abuse as seizures or arrhythmias may be precipitated.

Step 2: Take a Detailed History

- Detailed and targeted history from the family members and friends, including the past medical treatment and occupational environment, is important for making the diagnosis of poisoning.
- The history should include the type of toxin or toxins, time of exposure (acute versus chronic), amount taken, and route of administration (i.e., ingestion, intravenous, and inhalation).

Table 17.1 Physiological grading of the severity of poisoning: signs and symptoms

Severity	Stimulant poisoning	Depressant poisoning
Grade 1	Agitation, anxiety, diaphoresis, hyperreflexia, mydriasis, tremors	Ataxia, confusion, lethargy, weakness, verbal, able to follow commands
Grade 2	Confusion, fever, hyperactivity, hypertension, tachycardia, tachypnea	Mild coma (nonverbal but responsive to pain); brainstem and deep tendon reflexes intact
Grade 3	Delirium, hallucinations, hyperpyrexia, tachyarrhythmias	Moderate coma (respiratory depression, unresponsive to pain); some but not all reflexes absent
Grade 4	Coma, cardiovascular collapse, seizures	Deep coma (apnea, cardiovascular depression); all reflexes absent

- The patient should be asked about over-the-counter medications, vitamins, and herbal preparations.
- The patient or accompanying attendants should be asked about all drugs taken, including prescription drugs and empty bottles/containers, and the physician can also perform a “pill count” to ascertain the number of consumed pills.
- Remember the history of the patient may not always be forthcoming or reliable.
- The clinical diagnosis of the type of poisoning can be identified by the clinical manifestations that may fit into a particular toxidrome. Toxic overdose can present with a wide array of symptoms, including abdominal pain, vomiting, tremor, altered mental status, seizures, cardiac dysrhythmias, and respiratory depression, which may be the only clues to diagnosis (Table 17.1).
- Symptoms are often nonspecific (as in early acetaminophen poisoning) or masked by other conditions (e.g., myocardial ischemia in the setting of carbon monoxide poisoning).
- Consumption of multiple toxins may make the diagnosis challenging as the typical symptomatology may not be present.

Step 3: Perform Physical Examination

- The patient stabilization should take precedence over the detailed physical examination.
- Once the patient is stable, a more comprehensive physical and systemic examination should be performed.
- Serial examinations are even more important to assess dynamic change in clinical appearance. The systematic neurological evaluation is critical in patients with altered mental status. Alert/verbal/painful/unresponsive scale (AVPU) is a simple, rapid method of assessing consciousness in most poisoned patients.
- Focussed clinical examination, for example, characteristic odors of some poisoning (garlic in OP poisoning), pupillary findings, movement disorders like seizures, skin findings (flushed or pale, dry or warm), temperature alteration (hypo- or hyperthermia), respiratory alteration, etc., can help in differentiating types of poisonings.
- Look for features of associated trauma or injury during intoxication.

Step 4: Order Investigations

A basic metabolic panel should be obtained in all poisoned patients:

- Complete blood count
- Serum electrolytes
- Blood urea nitrogen and creatinine
- Blood glucose and bicarbonate level
- Liver functions test
- Coagulation profile
- Arterial blood gases (ABG)
- ABG with co-oximetry in patients with increased saturation gap or when dyshemoglobinemias are suspected
- ECG
- If the patient is a female of child-bearing age, a pregnancy test is essential.
- The anion gap, serum osmolality, and osmolar gap should be measured in each patient as it can help in finding the cause (Table 17.2).
- Chest and plain abdominal X-ray should be done if there is a high index of suspicion of radiopaque pills, drug-filled packets ie cocaine, enteric-coated tablets, heavy metals, etc.

Table 17.2 Common causes of abnormal anion gap

Elevated anion gap	Decreased anion gap	Increased osmolar gap
Lactic acidosis (type A)	Increased unmeasured cation	Methanol and ethylene glycol
Uremia	Hyperkalemia	Diabetic ketoacidosis (acetone)
Sepsis	Hypercalcemia	Isopropyl alcohol
Rhabdomyolysis	Hypermagnesemia	Ethanol
Ketoacidosis: diabetic, starvation, ethanol	Acute lithium intoxication	
	Elevated IgG (myeloma cationic paraprotein)	
	Decreased unmeasured anion	
	Hypoalbuminemia	
Toxic ingestions	Drugs	
Ethylene glycol	Bromide	
Methanol	Iodide	
Paraldehyde		
Salicylate	Polymyxin B	
	Analytical artifact	
	Hypernatremia	
	Hyperlipidemia	

Specific Investigations

- A sample for urine toxicology screening for common drugs must be taken before giving any sort of sedation.
- The cholinesterase level for organophosphorus poisoning: specific levels of cholinesterase can guide treatment.
- Paracetamol, salicylate, and other drug levels where appropriate.
- Oxygen saturation gap (SaO_2–SpO_2): An oxygen saturation gap is present when there is more than a 5% difference between the measured oxygen saturation from a standard blood gas machine and the reading from a pulse oximeter. If it is greater than 5%, the patient's hemoglobin may be abnormal, representing carbon monoxide poisoning (carboxyhemoglobin), methemoglobinemia (cyanide, dapsone), or sulfhemoglobinemia (hydrogen sulfide).

Step 5: Admit to the ICU

Admit in ICU if any of the following is present:

- Respiratory depression ($PaCO_2 > 45$ mmHg)
- Emergency intubation
- Seizures
- Cardiac arrhythmia (QT prolongation, preferably corrected QTc)
- QRS duration more than 0.12 ms
- Second- or third-degree atrioventricular block
- Systolic BP less than 80 mmHg
- Unresponsiveness to verbal stimuli
- Glasgow coma scale score less than 12
- Need for emergency dialysis, hemoperfusion, or extracorporeal membrane oxygenation
- Worsening metabolic acidosis
- Pulmonary edema induced by toxins (including inhalation) or drugs
- Tricyclic or phenothiazine overdose manifesting anticholinergic signs, neurologic abnormalities, QRS duration more than 0.12 s, or QT more than 0.5 s.
- Administration of pralidoxime in organophosphate toxicity
- Antivenom administration in envenomation
- Need for continuous infusion of naloxone

Step 6: Management

- The management of any clinically significant poisoning should begin with basic supportive measures. The priority after the airway, breathing, and circulation approach is to prevent and manage life-threatening complications.

Step 7: Decontamination

- The clothing should be removed in suspected or confirmed dermal exposures, and the skin should be copiously irrigated and washed with mild soap and water in organophosphorus poisoning.
- The eye should be copiously irrigated with water in ocular exposure to acids and alkali.
- Gastric lavage: The place of gastric lavage in acute poisoning is debatable and is only of benefit in the hyperacute phase of poisoning (<1 h). Caution: Patients must be awake with a preserved gag reflex or the airway should be secured before attempting gastric lavage.
- Activated charcoal: Charcoal aspiration has a high morbidity and mortality. This should not be attempted in patients without a safe or protected airway.
- Administer 50 g charcoal as soon as possible and another 50 g every 4 h thereafter while the indication persists. Co-administration with sorbitol has not been shown to increase efficacy.
- Charcoal administration is most effective when it is given within 1 h of ingestion.
- Contraindications to charcoal administration are as follows:
- Elemental metals (lithium, iron)
- Pesticides
- Strong acids or alkalis
- Cyanide
- Late presentations (>4–6 h post-ingestion)

Step 8: Enhanced Elimination

- Alkalinization of urine may help in the excretion of drug in the urine in poisonings such as salicylates, phenobarbital, and chlorpropamide.
- In cases of severe poisoning, dialysis and charcoal hemoperfusion should be considered if the toxin involved is removable through dialysis (see Fig. 17.1). Plasmapheresis has also been tried for removal of certain poisons (Table 17.3).
- Other therapies like extracorporeal membrane oxygenation (ECMO) for cardiac and pulmonary support have also been tried in several patients with acute poisoning (Table 17.3).
- Extracorporeal adsorption devices, such as Cytosorb, can be beneficial for treating overdoses of substances like amitriptyline, mercury, direct oral anticoagulants such as dabigatran, and ticagrelor.

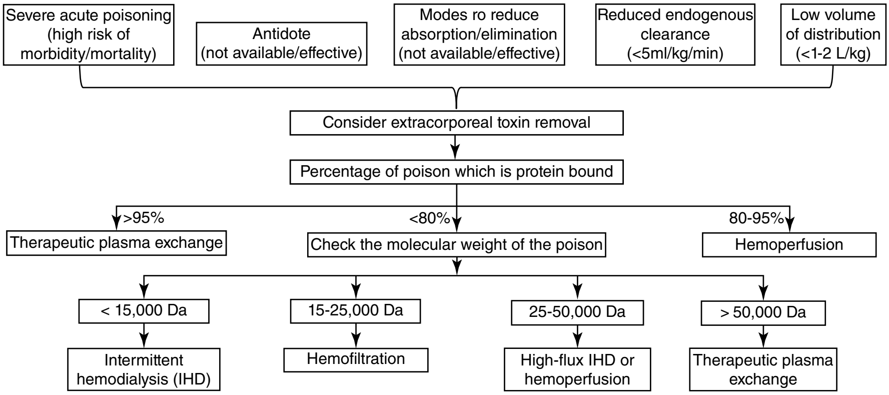
Severe acute poisoning (high risk of morbidity/mortality)
Antidote (not available/effective)
Modes ro reduce absorption/elimination (not available/effective)
Reduced endogenous clearance (<5ml/kg/min)
Low volume of distribution (<1-2 L/kg)
Consider extracorporeal toxin removal
Percentage of poison which is protein bound
>95%
<80%
80-95%
Therapeutic plasma exchange
Check the molecular weight of the poison
Hemoperfusion
< 15,000 Da
15-25,000 Da
25-50,000 Da
> 50,000 Da
Intermittent hemodialysis (IHD)
Hemofiltration
High-flux IHD or hemoperfusion
Therapeutic plasma exchange

Fig. 17.1 Approach to decide the mode for extracorporeal toxin removal

Table 17.3 Indication of dialysis and hemoperfusion

Hemodialysis	Hemoperfusion	Plasmapheresis	ECMO
Methanol	Theophylline	Tricyclic antidepressants	Amiodarone
Ethylene glycol	Phenobarbital	Thyroxine	Beta-blocker
Boric acid	Phenytoin	Heavy metals	Calcium channel blockers
Salicylates	Carbamazepine	Theophylline	Opioids
Lithium	Paraquat	Verapamil	Organophosphorus
	Glutethimide	Yellow phosphorus	Paraquat
Baclofen			Tricyclic antidepressants
Atenolol, sotalol			

Step 9: Use Antidotes to Common Poisons

- Antidotes should be used early in the course to counteract the effects of poisoning (Table 17.4).

Table 17.4 Common poisons and their antidotes

Poison	Antidote
Acetaminophen	*N*-Acetylcysteine
Anticholinergics	Physostigmine
Anticoagulants (warfarin/coumadin, heparin) Dabigatran Rivaroxaban, apixaban	Vitamin K, protamine, respectively Idramucizimab (praxbind) Adenaxet alfa
Benzodiazepines	Supportive care, flumazenil
Botulism	Botulinum antitoxin
β-Blockers	Glucagon
Calcium channel blockers	Calcium, glucagon
Cholinergic (i.e., organophosphorus)	Atropine, pralidoxime
Carbon monoxide	Oxygen, hyperbaric oxygen
Cyanide	Amyl nitrate, sodium nitrate, sodium thiosulfate, hydroxocobalamin
Digoxin	Digoxin Fab antibodies
Iron	Desferrioxamine
Isoniazid	Pyridoxine
Lead	BAL, EDTA, DMSA
Methemoglobinemia	Methylene blue
Opioids	Naloxone
Toxic alcohols	Ethanol drip, dialysis Fomepizole
Tricyclic antidepressants	Sodium bicarbonate

[a] Use of flumazenil may be contraindicated in many situations including tricyclic overdose or in chronically habituated benzodiazepine users as this may precipitate seizures

Step 10: Other Measures

Intravenous fat emulsion (IFE) has been suggested as a potentially beneficial therapy in the management of local anesthetic overdose. For example, bupivacaine, mepivacaine, ropivacaine, levobupivacaine, prilocaine, lignocaine, and lidocaine. It has also been tried in several other poisoning, with varied results (Table 17.5). While the exact mechanism of action is not fully understood, it is believed that the antidote may work by compartmentalizing the offending drug into a lipid phase, thereby sequestering it away from its target receptors.. As per the current dosing recommendations, a bolus of 1.5 mL/kg, followed by an intravenous infusion at the rate of 0.25 mL/kg/min, should be initiated.

Step 11: Whenever in Doubt, Seek Help from the National Poison Information Centre (AIIMS)

Table 17.5 Drug toxicities that may benefit from the use of intravenous fat emulsion

Probable benefit
All local anesthetics: bupivacaine, mepivacaine, ropivacaine, levobupivacaine, prilocaine, lignocaine, lidocaine

Possible benefit
Anti-epileptics: carbamazepine, lamotrigine
Anti-psychotics: chlorpromazine, haloperidol, olanzapine, quetiapine
Anti-histamine: diphenhydramine
Barbiturates: pentobarbital, phenobarbital, thiopental
Beta-blockers: atenolol, carvedilol, metoprolol, nebivolol, propranolol
Calcium channel blockers: amlodipine, diltiazem, felodipine, nifedipine, verapamil
Disease-modifying antirheumatic drug: hydroxychloroquine
Tricyclic antidepressants: amitriptyline, clomipramine, dosulepin, dothiepin, doxepin, imipramine
Other antidepressants: bupropion, venlafaxine
Others: baclofen, cocaine, endosulfan, flecainide, propanone

Suggested Reading

American College of Medical Toxicology. ACMT position statement: interim guidance for the use of lipid resuscitation therapy. J Med Toxicol. 2011;7:81–2. *A statement on the use of lipids in poisonings.*

Bouchard J, Shepherd G, Hoffman RS, Gosselin S, Roberts DM, Li Y, et al; EXTRIP workgroup. Extracorporeal treatment for poisoning to beta-adrenergic antagonists: systematic review and recommendations from the EXTRIP workgroup. Crit Care. 2021;25(1):201. https://doi.org/10.1186/s13054-021-03585-7. *EXTRIP guidelines for the use of extracorporeal therapies in the management of beta-blocker toxicity.*

Boyle JS, Bechtel LK, Holstege CP. Management of the critically poisoned patient. Scand J Trauma Resusc Emerg Med. 2009;17:29. *If a poisoning is recognized early and appropriate testing and supportive care is initiated early, it will improve outcome. It is important to understand the indications and contraindications of antidotes prior to its use.*

Freund Y, Viglino D, Cachanado M. Effect of noninvasive airway management of comatose patients with acute poisoning: a randomized clinical trial. JAMA. 2023;330(23):2267–74. *A randomized study of intubation vs noninvasive airway management of overdose patient with poor GCS had shown benefit of expectant watching.*

Ghannoum M, Roberts DM, Hoffman RS, Ouellet G, Roy L, Decker BS, Bouchard J. A stepwise approach for the management of poisoning with extracorporeal treatments (ECTRs). Semin Dial. 2014;27:362–70. *A detailed understanding of the capabilities and limitations of the different ECTRs can be useful to select the most appropriate ECTR for a given clinical situation.*

Jaffal K, Chevillard L, Mégarbane B. Lipid emulsion to treat acute poisonings: mechanisms of action, indications, and controversies. Pharmaceutics. 2023;15(5):1396. https://doi.org/10.3390/pharmaceutics15051396. *Intravenous fat emulsion may be an effective antidote in poisonings from various xenobiotics.*

Kobylarz D, Noga M, Frydrych A, Milan J, Morawiec A, Glaca A, et al. Antidotes in clinical toxicology-critical review. Toxics. 2023;11(9):723. https://doi.org/10.3390/toxics11090723. *Comprehensive and updated list of toxins and their antidotes*

Ouellet G, Bouchard J, Ghannoum M, Decker BS. Available extracorporeal treatments for poisoning: overview and limitations. Semin Dial. 2014;27(4):342–9. *This article discusses the overview of extracorporeal treatments (ECTRs) like intermittent hemodialysis, sustained low-efficiency dialysis, intermittent hemofiltration and hemodiafiltration, continuous renal replacement therapy, hemoperfusion, therapeutic plasma exchange, exchange transfusion, peritoneal dialysis, albumin dialysis, and cerebrospinal fluid exchange in poisonings.*

Thanacoody R, Caravati EM, Troutman B, Höjer J, Benson B, Hoppu K, et al. Position paper update: whole bowel irrigation for gastrointestinal decontamination of overdose patients. Clin Toxicol (Phila). 2015;53(1):5–12. https://doi.org/10.3109/15563650.2014.989326. *Recommendations for whole bowel irrigation in managing patients with acute poisoning.*

Drug Abuse

18

Deven Juneja, Omender Singh, and Prashant Nasa

A 38-year-old male known alcohol abuser, chronic smoker, and IV drug abuser came to the emergency department in an inebriated state. On examination, he was cachectic and stuporous with bilateral pinpoint pupils. There were multiple black erythematous patches on the forearm with multiple injection marks. His pulse rate was 46/min and blood pressure was 82/60 mmHg, and on auscultation, there were bilateral crepitations.

Substance abuse may be persistent or sporadic, and inconsistent with or unrelated to acceptable medical practice. This subset of patients may present to the hospital with acute intoxication, withdrawal, or infectious and other chronic complications related to drug abuse. They have an overall better prognosis compared to other critically ill patients if diagnosed and managed timely. Narcotics, stimulants, and sedatives are the common prescription drugs of abuse. Patients may present with deliberate or accidental overdose.

Step 1: Initiate resuscitation

- Initial resuscitation should be done as mentioned in Chap. 24, Vol. 2.

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- In addition to routine investigations, CT head should be done to rule out intracranial bleeding in patients presenting with hypertension, particularly with stimulant abuse (e.g., cocaine).
- Administer IV naloxone in cases of suspected opioid-induced respiratory depression as it can quickly reverse the effects and potentially prevent the need for intubation. However, use caution in patients with a history of chronic opioid abuse as naloxone may trigger withdrawal symptoms, including seizures and arrhythmias.

Airway

- Management of airways is very important in poisoning. When intubation is necessary, rapid sequence induction is indicated using short-acting paralytic agents.
- Urine toxicology screening should be obtained before administering any sedatives or hypnotics.
- In a recent multicenter study, a strategy of withholding intubation in patients with Glasgow coma scale less than 9, due to overdose with sedatives, narcotics, etc. was associated with a reduction in mortality.

Breathing

- Patient's oxygenation status can be monitored with a bedside pulse oximeter.
- Give oxygen by the nasal cannula or facemask to maintain SpO_2 of more than 95%.
- Patient should be started on assisted ventilation if unable to maintain oxygenation or ventilation.

Circulation

- Monitor pulse and blood pressure and do ECG.
- Obtain a wide-bore peripheral line and start intravenous fluids.

Step 2: Initial Assessment

- This subset of patients may present to the hospital with acute intoxication, withdrawal, or infectious and other chronic complications related to drug abuse. The drugs of abuse can be classified into major groups as given in Table 18.1.
- The initial evaluation of these patients has multiple physical, social, emotional, and medicolegal issues that should be addressed.

Table 18.1 Classification of drugs of abuse

Class	Drugs/toxins
Stimulants	Amphetamines, methamphetamine, cocaine, 3,4-methylenedioxymethamphetamine, nicotine, caffeine
Depressants	Barbiturates, benzodiazepines, gamma-hydroxybutyrate, antihistaminics
Hallucinogens	Lysergic acid diethylamide, mescaline, psilocybin (mushrooms), dextromethorphan
Dissociative anesthetics	Ketamine, phencyclidine, and analogs (angel dust)
Cannabinoids	Ganja, hashish, marijuana
Opiates	Opium, heroin, morphine, fentanyl, codeine, oxycodone, tramadol
Inhalants	Acetone, aerosol sprays, paint thinner, gases (nitrous oxide), glue, amyl nitrite, gasoline, Iodex, pen ink, marker, room deodorizers
Others	Alcohol, anabolic steroids
Newer drugs	Substituted cathinone, synthetic cannabinoids, piperazines, substituted phenethylamines, kratom, tryptamines, salvia

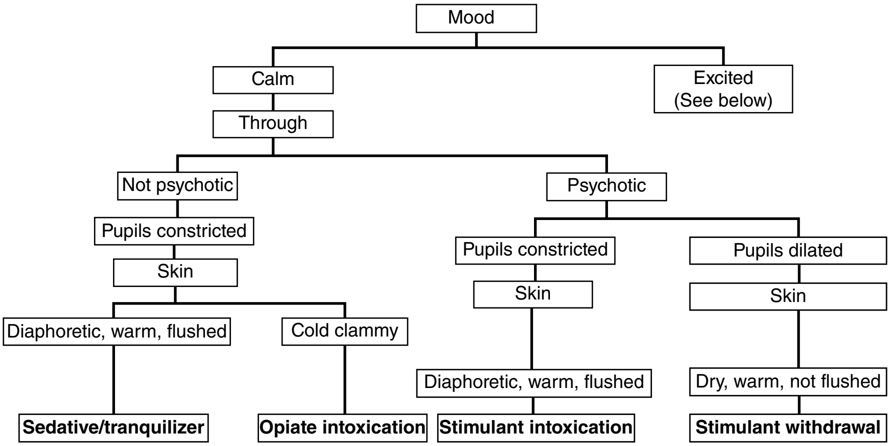
Mood
Calm
Excited (See below)
Through
Not psychotic
Psychotic
Pupils constricted
Skin
Diaphoretic, warm, flushed
Cold clammy
Pupils constricted
Skin
Pupils dilated
Skin
Diaphoretic, warm, flushed
Dry, warm, not flushed
Sedative/tranquilizer
Opiate intoxication
Stimulant intoxication
Stimulant withdrawal

Fig. 18.1 Algorithm for the diagnosis of drug intoxication and withdrawal

History

- Complete and focused history should be taken from the patient, family, accompanying physician, or police, as mentioned in Chap. 6, Vol. 2. However, history may not be forthcoming or reliable in such cases.
- Perform detailed clinical examination (Figs. 18.1 and 18.2):
  - Once the patient is stable, a more comprehensive physical and systemic examination should be performed.

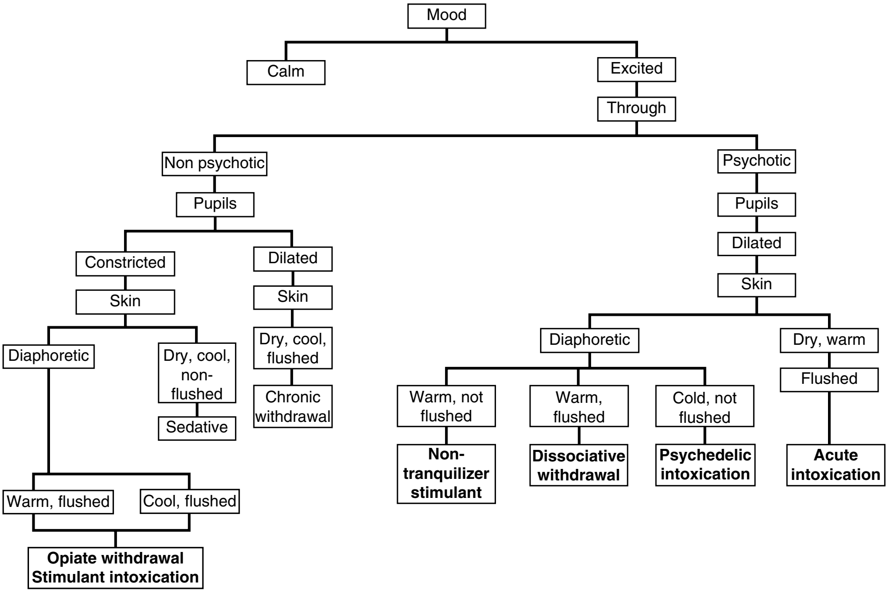
Mood
Calm
Excited
Through
Non psychotic
Psychotic
Pupils
Constricted
Dilated
Skin
Diaphoretic
Dry, cool, non-flushed
Sedative
Dry, cool, flushed
Chronic withdrawal
Warm, flushed
Cool, flushed
Opiate withdrawal Stimulant intoxication
Pupils
Dilated
Skin
Diaphoretic
Dry, warm
Flushed
Warm, not flushed
Warm, flushed
Cold, not flushed
Non-tranquilizer stimulant
Dissociative withdrawal
Psychedelic intoxication
Acute intoxication

Fig. 18.2 Algorithm for the diagnosis of drug intoxication and withdrawal (continued)

- Serial examinations are even more important to assess dynamic change in clinical appearance.
- The systematic neurological evaluation is particularly important in patients with altered mental status. Alert/verbal/painful/unresponsive scale (AVPU) is a simple and rapid method of assessing consciousness in most poisoned patients.

Step 3: Diagnosis by Toxidromic Approach

The signs and symptoms of drugs of abuse are organized around the activity of six neurotransmitters (Table 18.2). This activity is sufficiently unique to permit rapid identification of the specific drug responsible for a given clinical situation.

- Based on history and examination, it may be possible to define a constellation of signs and symptoms or toxidromes, which may help in diagnosing the unknown poison and provide a specific antidote. Polydrug abuse is common and may complicate the clinical picture and make the diagnosis more challenging.

Table 18.2 Specific treatment for intoxication, overdose, and withdrawal based on the affected neurotransmitter

Neurotransmitters involved in intoxication	Treatment
Acetylcholine	Physostigmine
β-Endorphin	Naloxone (Narcan)
Dopamine	Benzodiazepine
	Butyrophenone
GABA	Mechanical support
Norepinephrine	β-Blocker
	Benzodiazepine
Serotonin	Benzodiazepine
Withdrawal	
β-Endorphin	Methadone, clonidine
Dopamine	Bromocriptine
GABA	Barbiturate or benzodiazepine replacement
Norepinephrine	Desipramine
Serotonin	Fluoxetine

GABA gamma-aminobutyric acid

Step 4: Diagnose Common Drug Abuse

A. Alcohol

- Acute effects:
  - Central nervous system (CNS) depressant.
  - In low doses, alcohol depresses inhibitory centers and resultant disinhibition (out-of-character activities).
  - At higher doses, alcohol inhibits excitatory centers.
- Signs of chronic alcohol abuse:
  - Gastrointestinal—liver cirrhosis, peptic ulcer disease, gastritis, pancreatitis, and carcinoma
  - Cardiovascular—hypertension, cardiomyopathy, atrial fibrillation (“holiday heart syndrome”)
  - Neurological—peripheral neuropathy leading to ataxia, Wernicke encephalopathy, Korsakoff psychosis, and structural changes in the brain leading to dementia
  - Immunologic—suppression of neutrophil function and cell-mediated immunity
  - Endocrine—in males, increase in estrogen and a decrease in testosterone, leading to impotence, testicular atrophy, and gynecomastia
- Psychiatric—depression or anxiety disorders

B. Opiates
  - Acute intoxication—decreased respiratory rate and pinpoint pupils, with complications including noncardiogenic pulmonary edema and respiratory failure.
  - Complications of chronic abuse are primarily infectious and include skin abscess at an injection site, cellulitis, mycotic aneurysms, endocarditis, talcosis, HIV, and hepatitis.

C. Cocaine

  Cocaine may be smoked, inhaled, used topically, or injected:
  - Acute cocaine intoxication may present with agitation, paranoia, tachycardia, tachypnea, hypertension, and diaphoresis.
  - Complications of acute and chronic use can include myocardial ischemia or infarction, stroke, pulmonary edema, and rhabdomyolysis.

D. Amphetamines
  - Acute intoxication with amphetamines presents with signs of sympathetic nervous system stimulation, tachycardia, hypertension, anorexia, insomnia, and occasionally seizures.

E. Hallucinogens
  - Different hallucinogens present with a variety of organ system effects.
  - Phencyclidine (PCP) has been known to cause muscle rigidity, seizures, rhabdomyolysis, and coma.
  - Anticholinergics have been associated with delirium, supraventricular tachycardia, hypertension, and seizures.

Other hallucinogens (e.g., lysergic acid diethylamide, peyote, marijuana, and nutmeg) rarely cause significant physical complications.

Step 5: Send Investigations

A basic metabolic panel should be obtained in all suicidal poisoned patients:
- Complete blood count
- Serum electrolytes
- Blood urea nitrogen, creatinine
- Liver function tests
- Blood glucose, bicarbonate level
- Arterial blood gases
- ECG
- Echocardiography

  Special investigations:
- Urine toxicology screening: In patients with acute intoxication, urine screening for substances of abuse and a blood or breath alcohol level may be considered, but these generally do not alter management. Urine toxicology screening is needed for the following:

  - Amphetamines
  - Barbiturates
  - Benzodiazepines
  - Cannabinoids
  - Cocaine
  - Opioids
  - Phencyclidine
- Caution: a single negative urine toxicology screening or urine immunoassay is not reliable, and repeat tests should be done after a few hours especially if clinical suspicion is high:
  - Blood toxicology profile, if available.
  - If the patient is a female of child-bearing age, a pregnancy test is essential.
  - Serum ethanol level, anion gap, serum osmolality, and osmolar gap should be performed for alcohol intoxication.
  - A CT scan of the head is advised if altered mental status is not explained or in the presence of new focal neurological deficit.

Step 6: General Management

- The general principle of management of patients with suspected drug overdose or withdrawal is supportive and includes standard resuscitative measures, employing the ABCDE approach.
- Once the patient has been stabilized, the physician must consider how to minimize the bioavailability of toxin not yet absorbed, which antidotes (if any) to administer, and what other measures should be undertaken to enhance elimination.
- After initial resuscitation, use the specific antidote, when available.

The management of acute intoxication and withdrawal again will depend on the particular neurotransmitters involved (Table 18.2).

Step 7: Manage as per Specific Class

A. Dissociative drugs
  - *Acute intoxication*: haloperidol, a presynaptic dopamine antagonist, is useful for blocking significant symptoms of dissociative intoxication.
  - *Dose*: 1 mg IV every 15–20 min, up to maximum 10 mg. This can be given orally or intramuscularly, too.

Alternative to haloperidol is risperidone.
  - *Chronic intoxication*: desipramine for post-withdrawal depression.

B. Opiates
  - *Specific antidote* (naloxone, naltrexone, naltrefene): naloxone, at a dose of 0.1–0.4 mg or 0.01 mg/kg IV, may have to be repeated every 1–2 min.

- *Naloxone* should not be used in patients with chronic abuse as it can precipitate seizures or withdrawal.
- *Withdrawal*: Methadone is the drug of choice, but not easily available. Clonidine orally or through Ryle's tube (17 μg/kg/day in three to four doses) can be used.

C. Hallucinogens
- *Acute intoxication*: benzodiazepines (midazolam, diazepam, alprazolam) are the drugs of choice.
- *Withdrawal*: fluoxetine can be given orally.

D. Sedative–hypnotic drugs
- *Acute intoxication*: for supportive management, flumazenil is the specific antidote for benzodiazepines but can precipitate seizures or withdrawal in patients with chronic abuse.
- *Chronic intoxication/withdrawal*:

  Barbiturates: The equivalent dose of phenobarbitone for a period, which depends on the duration of action of the abused drug for withdrawal effect. Flumazenil can cause seizures in patients with chronic intoxication of barbiturates.

  Benzodiazepines: Long-acting drugs like chlordiazepoxide (Librium) orally or through Ryle's tube (maximum up to 25 mg, three to four times a day), or lorazepam (1–2 mg three to four times a day) may be prescribed.

  Alcohol: Same as benzodiazepines. If chronic abuse, give thiamine 200 mg.

E. Stimulant drugs
- *Acute intoxication*: benzodiazepines (lorazepam) are the drugs of choice.
- *Chronic abuse*: bromocriptine and/or desipramine can be given orally.
- Patients with substance abuse may present to the hospital with acute intoxication, withdrawal, or infectious and other chronic complications related to drug abuse.
- Initial resuscitation should be done using the ABCDE approach.
- Based on detailed history and clinical examination, it may be possible to define a constellation of signs and symptoms or toxidromes, which may help in diagnosing the unknown poison.
- Specific investigations may be required to diagnose specific substance abuse.
- After initial resuscitation, use the specific antidote when available.

Suggested Reading

Betten DP, Vohra RB, Cook MD, Matteucci MJ, Clark RF. Antidote use in the critically ill poisoned patient. J Intensive Care Med. 2006;21(5):255–77. *The more commonly used antidotes that may be encountered in the intensive care unit (N-acetylcysteine, ethanol, fomepizole, physostigmine, naloxone, flumazenil, sodium bicarbonate, octreotide, pyridoxine, cyanide antidote kit, pralidoxime, atropine, digoxin immune Fab, glucagon, calcium gluconate and chloride, deferoxamine, phytonadione, botulism antitoxin, methylene blue, and Crotaline snake antivenom) are reviewed*

Clinical Guideline Committee (CGC) Members; ASAM Team; AAAP Team; IRETA Team. The ASAM/AAAP Clinical Practice Guideline on the Management of Stimulant Use Disorder. J Addict Med. 2024;18(1S Suppl 1):1–56. https://doi.org/10.1097/ADM.0000000000001299. *The guidelines discuss in detail the management of patients with stimulant abuse*

Freund Y, Viglino D, Cachanado M, Cassard C. Effect of noninvasive airway management of comatose patients with acute poisoning: a randomized clinical trial. JAMA. 2023;330(23):2267–74. *Withholding intubation in patients with Glasgow coma scale less than 9, due to overdose with sedatives, narcotics, etc., was associated with a reduction in mortality*

Holstege CP, Borek HA. Toxidromes. Crit Care Clin. 2012;28(4):479–98. *This article reviews the general approach to the poisoned patient, specifically focusing on the utility of the toxidrome. A toxidrome is a constellation of findings, either from the physical examination or from ancillary testing, which may result from any poison. There are numerous toxidromes defined in the medical literature. This article focuses on the more common toxidromes described in clinical toxicology*

Marraffa JM, Cohen V, Howland MA. Antidotes for toxicological emergencies: a practical review. Am J Health Syst Pharm. 2012;69(3):199–212. *This review highlights the role pharmacists can play a key role in reducing poisoning and overdose injuries and deaths by assisting in the early recognition of toxic exposures and guiding emergency personnel on the proper storage, selection, and use of antidotal therapies*

Moeller KE, Kissack JC, Atayee RS, Lee KC. Clinical interpretation of urine drug tests: What clinicians need to know about urine drug screens. Mayo Clin Proc. 2017 Mar 18. pii: S0025-6196(16)30825-4. *In this report, technical information related to detection methods of urine drug tests that are commonly used is provided, and an overview of false-positive/false-negative data for commonly misused substances in the following categories: cannabinoids, central nervous system (CNS) depressants, CNS stimulants, hallucinogens, designer drugs, and herbal drugs of abuse are given. Brief discussions of alcohol and tricyclic antidepressants as related to urine drug tests are described. The goal of this review was to provide a useful tool for clinicians when interpreting urine drug test results and making appropriate clinical decisions on the basis of the information presented*

The ASAM National Practice Guideline For the Treatment of Opioid Use Disorder: 2020 Focused Update. https://sitefinitystorage.blob.core.windows.net/sitefinity-production-blobs/docs/default-source/guidelines/npg-jam-supplement.pdf?sfvrsn=a00a52c2_2. Assessed 4 Aug 2024. *These guidelines from the American Society of Addiction Medicine describes the different types of drug dependance and focuses on the diagnosis and management of patients with opiod use disorder*

Snakebite

19

Dhruva Chaudhry, Jaideep Phougat, and Aman Dhankar

Case Vignette

Case 1: A 20-year-old man presented with a history of diffuse abdominal pain, myalgias, difficulty in swallowing, and pooling of secretions. He also complained of difficulty in breathing and diplopia with acute onset drooping of eyes. He was conscious, and oriented to time and space, with a respiratory rate of 12/min and a single breath count of 12. The power in all limbs was 4/5, but all reflexes were absent. He had ptosis, and the rest of the general and systemic examination was normal. He was absolutely normal the previous night when he had slept on the floor.

Case 2: A 36-year-old male farmer presented to the emergency department with swelling and bleeding from the left leg after he was bitten early in the morning when he was working on the farm. He also complained of bleeding from gums, hematuria, and not passing urine since morning. He was conscious and oriented. His blood pressure was 90/60 mmHg. A neurological examination did not reveal any abnormality.

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Snakebite is an injury caused by a bite from a snake that sometimes results in envenomation. Most of the snakes are nonvenomous. Some snakebites result in envenomation. The outcome of snakebite depends on numerous factors that include the species of snake, the area of the body bitten, and the amount of venom injected.

Step 1: Initial Resuscitation and Assessment

Airway

- Management of the airway is very important in neuroparalytic snakebite.
- The patient should be assessed for any pooling of secretions, inability to open mouth or protruding tongue, and weakness of neck flexors (broken neck sign). Patients with any of these signs or a single breath count of <10 should be immediately intubated following the standard procedure of intubation.

Breathing

- The patient's oxygenation status can be monitored with a bedside pulse oximeter. Supplemental oxygen should be given in the presence of hypoxia.
- When the patient is in respiratory distress and not able to maintain oxygenation, he/she should be put on assisted ventilation.

Circulation

- Obtain a good peripheral line and start intravenous fluids. Start vasopressors if hypotension persists after adequate fluid resuscitation.
- Be careful while venipuncture in patients with coagulopathy.

Step 2: Take a Detailed History (Table 19.1)

- Detailed history should be taken such as the type of the snake (species), timing of bite, what was he/she doing at that time, location (in which part of the body the snake has bitten), and first-aid measures received.
- Patients with snakebite usually present with a history of sudden onset of generalized weakness, abdominal pain, and vomiting.
- Neurological symptoms include drooping of eyelids, blurred or double vision, difficulty in swallowing, pooling of secretions, and difficulty in breathing (4Ds—diplopia, dysphagia, dysphonia, dyspnea).
- Ask for local swelling or pain in the body and bleeding from any site.

Table 19.1 Syndromes associated with snakebite

Local effects	Vipers, cobra, sea snakes (usually absent in krait)
Coagulopathy	Vipers (Russell's viper, hump-nosed viper, saw-scaled viper)
Neurotoxicity	Cobra, common krait, sea snakes, Russell's viper (in some cases)
Renal toxicity	Russell's viper, hump-nosed viper
Myotoxicity	Sea snakes, some krait species

Table 19.2 Differential diagnosis of acute neurological weakness

Acute inflammatory demyelinating polyradiculoneuropathy (AIDP, i.e., LGB syndrome)
Transverse myelitis
Periodic paralysis (hypokalemic, hyperkalemic, normokalemic)
Acute myasthenic crisis
Organophosphorus poisoning
Hypomagnesemia and hypophosphatemia
Hypoglycemia
Acute intermittent porphyrias
Polymyositis/dermatomyositis
Tick paralysis
Head/spinal cord injury

Step 3: Perform Physical Examination

- A comprehensive general physical and neurological examination should be performed on all patients with suspected snakebite.
- The examination may reveal generalized motor weakness with sluggish deep tendon reflexes.
- There may be ptosis and both internal and external ophthalmoplegia giving a false impression of brain stem dysfunction. However, the patient responds to commands by using the frontalis muscle and orbicularis oculi.
- Usually, there are no local reactions in neuroparalytic snake envenomation (krait); however, in cobra bite, severe local reactions can be seen.
- The differential diagnosis of any patient presenting with sudden onset of neurological deficit with respiratory compromise is enumerated in Table 19.2.
- Examination of the bitten part: fang marks, extent of swelling, blisters, necrosis, infection, and abscess formation (Table 19.3).
- Bleeding from the bite site may be the first manifestation of envenomation.
- Look for hematuria, epistaxis, bleeding from gums, hematemesis, and ecchymosis.
- Check blood pressure and carefully follow and monitor.

Table 19.3 Symptoms and signs of snakebite

Local	Fang marks, swelling, blisters, necrosis, bleeding from bite site, lymph node enlargement, infection, abscess formation, and compartmental syndrome.
Neurological	Diplopia, ptosis, cranial nerve palsies, dysphagia, dysphonia, pooling of secretions, neck muscle weakness, respiratory muscle weakness, paradoxical breathing, descending paralysis, diminished, or absent deep tendon reflexes.
Coagulopathy	Bleeding from bite site, bleeding from gums, epistaxis, hemoptysis, hematemesis, retroperitoneal bleeding, and intracranial bleeding resulting in various neurological manifestations.
Renal	Loin pain, hematuria, hemoglobinuria, myoglobinuria, oliguria/anuria. Symptoms and signs of AKI.
Cardiovascular	Visual disturbances, faintness, collapse, hypotension, shock, arrhythmias, myocardial damage. Generalized increase in vascular permeability resulting in facial, periorbital edema, conjunctival edema, pleural and pericardial effusions, haemoconcentration, and albuminuria.
Skeletal muscle	Generalized pain, stiffness and tenderness of muscles, pain on passive stretching, trismus, and myoglobinuria.
Others	Fear, anxiety, nausea, vomiting, abdominal pain, weakness, and drowsiness. Stroke due to arterial thrombosis. Acute pituitary or adrenal insufficiency.

Table 19.4 Severity of snakebite

Severity	Local findings	Systemic findings
Nonenvenomation (dry bite)	None or puncture wounds only	None
Mild	Puncture wounds, pain, soft tissue swelling confined to the bite site	None
Moderate	Swelling beyond bite site	Mild nausea, vomiting or fasciculations, paraesthesia, microscopic hematuria
Severe	Severe pain and swelling	Respiratory failure or hypotension or bleeding

Step 4: Severity of Snakebite

Once a diagnosis of snakebite is made, the patient should be assessed for the severity, as enumerated in Table 19.4.

Step 5: Order Investigations

- Complete hemogram with platelet counts, bleeding time (BT), coagulation time (CT), and 20 min whole blood clotting test (20WBCT).
- Urine examination—RBCs in the presence of gross hematuria.
- Prothrombin time, INR, PTTK, fibrinogen level, fibrin degradation product, D-dimer.

Table 19.5 Admission to the ICU

Circulatory shock, cardiac dysfunction, pulmonary edema
Hemorrhage, hypovolemia
Coagulopathy, disseminated intravascular coagulation
Coma, seizures, intracranial hemorrhage
Cranial nerve dysfunction
Rhabdomyolysis, renal failure, hyperkalemia
Gastrointestinal bleeding
Respiratory failure
Anaphylaxis (component of venom or antivenom)

- If urine is smoky, dipstick positive for blood and RBCs absent, look for myoglobulin to rule out myoglobinuria.
- Blood urea and serum creatinine levels should be regularly monitored in patients with renal failure.
- Serum electrolytes and blood gas analysis.
- ECG for arrhythmias.
- Aminotransferases and muscle enzymes (creatine kinase and aldolase).

Step 6: Admit to the ICU

- Indications of ICU admission are mentioned in Table 19.5.

Step 7: General Management

- All the patients should receive antitetanus toxoid and the local wound should be cleaned with soap and water.
- In patients with coagulopathy, tetanus prophylaxis should be postponed until after antivenom therapy.
- The limb with the bite mark should be immobilized; however, no tourniquet should be tied except in conditions where transport to a higher center will be prolonged, pressure bandage may be applied rather than immobilization alone.
- Keep the bitten limb lower than the heart as far as possible.
- Open the tourniquet, if applied outside, only when resuscitative measures are available and ideally after administration of anti-snake venom.
- Patients with mild features should be observed for at least 24 hours.
- Do not apply ice to the bite site. Avoid vigorous cleaning, incision, or suctioning to bite site.
- Routine use of antibiotics is not recommended.
- Measure intracompartmental pressure if compartmental syndrome is suspected.
- Monitor blood pressure, oxygenation, cardiac rhythm, and urinary output.

Step 8: Specific Management

Antisnake Venom

- Antisnake venom (ASV) is prepared from horses' serum.
- It can be monovalent or polyvalent.
- One milliliter of reconstituted polyvalent antivenin neutralizes 0.6-mg venom of Indian cobra and Russell's viper and 0.45 mg of common krait and saw-scaled viper.
- ASV should not be administered locally at the bite site.
- The usual initial dose of ASV is 10 vials.
- ASV can be given either by slow injection (maximum 2 ml/min) or by intravenous infusion (diluted in normal saline or dextrose -5 ml/kg body weight) over 30–60 min.
- Repeat the initial dose of ASV if blood remains noncoagulable after 6 hours, or 1 hour later if spontaneous bleeding persists, or neurotoxic or cardiovascular signs persist or deteriorate.
- Children should be given the same dose of ASV as adults since the amount of venom injected is same.
- ASV will not have a dramatic effect in neuroparalysis. Low-dose ASV is as effective as high dosage in neuroparalytic snake envenomation.
- ASV will however have a dramatic effect in stopping bleeding in coagulation abnormalities.
- Seek expert help if unfamiliar with the administration of ASV.
- Patients with confirmed snakebite and evidence of life-threatening systemic envenomation should receive ASV (Tables 19.3 and 19.4).

Step 9: Watch for Reaction

- ASV is a foreign protein. Therefore, allergic reactions including anaphylaxis are not unknown.
- Skin test before injection is not recommended to predict infusion reactions.
- H_1 blockers, H_2 blockers, and hydrocortisone do not decrease the incidence of infusion reactions.
- Use of prophylactic adrenaline 0.25 mg (0.25 ml of 1% adrenaline given subcutaneously) is recommended to decrease the incidence of infusion reactions, especially in situations where there may be a high risk of allergic reactions or resuscitative measures not available if it occurs.

- An adrenaline syringe should always be kept ready before infusing ASV.
- If the patient develops a reaction to ASV during infusion, first stop the infusion of ASV.
- It should be followed by adrenaline—the usual recommended dosage is 0.5 mg of 1:1000 dilutions intramuscularly.
- Additional dosages of H_1 (chlorpheniramine maleate) and H_2 (ranitidine) blockers with hydrocortisone 100 mg, though later will take 4–6 h to act, should be given simultaneously.
- If needed, adrenaline can be repeated up to two to three dosages or an infusion can be started in dilution of 1:50,000.
- Hypotension is treated with fluids. Inotropes may be required in patients who had overt myocardial dysfunction.
- There are no absolute contraindications to ASV but should be used with caution in patients with asthma, on beta-blocker or ACE inhibitors.

Step 10: ICU Management

- Initiate mechanical ventilation at the appropriate time as it reduces the mortality significantly in neuroparalytic envenomation.
- Anticholinesterase drugs such as edrophonium and neostigmine have also been recommended for the treatment of neuroparalytic snake envenomation for envonomation with postsynaptic neurotoxicity. They should be given with atropine to take care of their harmful effect.
- 10 mg of edrophonium (IV) or 0.5 mg of neostigmine (IM) should be given over 2–3 min with atropine pretreatment (0.6 mg). In case the patient improves, he/she should be managed with neostigmine/atropine over the next 24–48 h.
- If there is no improvement after 3 doses of atropine neostigmine (within 1 h), this indicates probable Krait bite. Krait affects presynaptic fibres where calcium ion acts as neurotransmitter. Give Inj. Calcium gluconate 10 ml IV [in children 1–2 ml/kg (1:1 dilution)] slowly over 5–10 min every 6 hourly and continue till neuroparalysis recovers that may last for 5–7 days.
- General ICU management—propped up nursing, ulcer prophylaxis, DVT prophylaxis, glucose control and appropriate sedation, and analgesia.
- Majority of patients usually recover within 48 h.

Step 11: Manage Complications

- Patients who develop complications should be managed in the ICU till they are resolved (Table 19.5).
- Consider wound debridement if local swelling and necrosis is severe enough to threaten viability of the limb and life.
- Consider fasciotomy if there is clinical evidence of intracompartmental syndrome or when the intracompartmental pressure exceeds 40 mmHg (in adults).
- Rhabdomyolysis should be managed with adequate hydration, correction of acidosis with bicarbonate, and promoting alkaline diuresis.

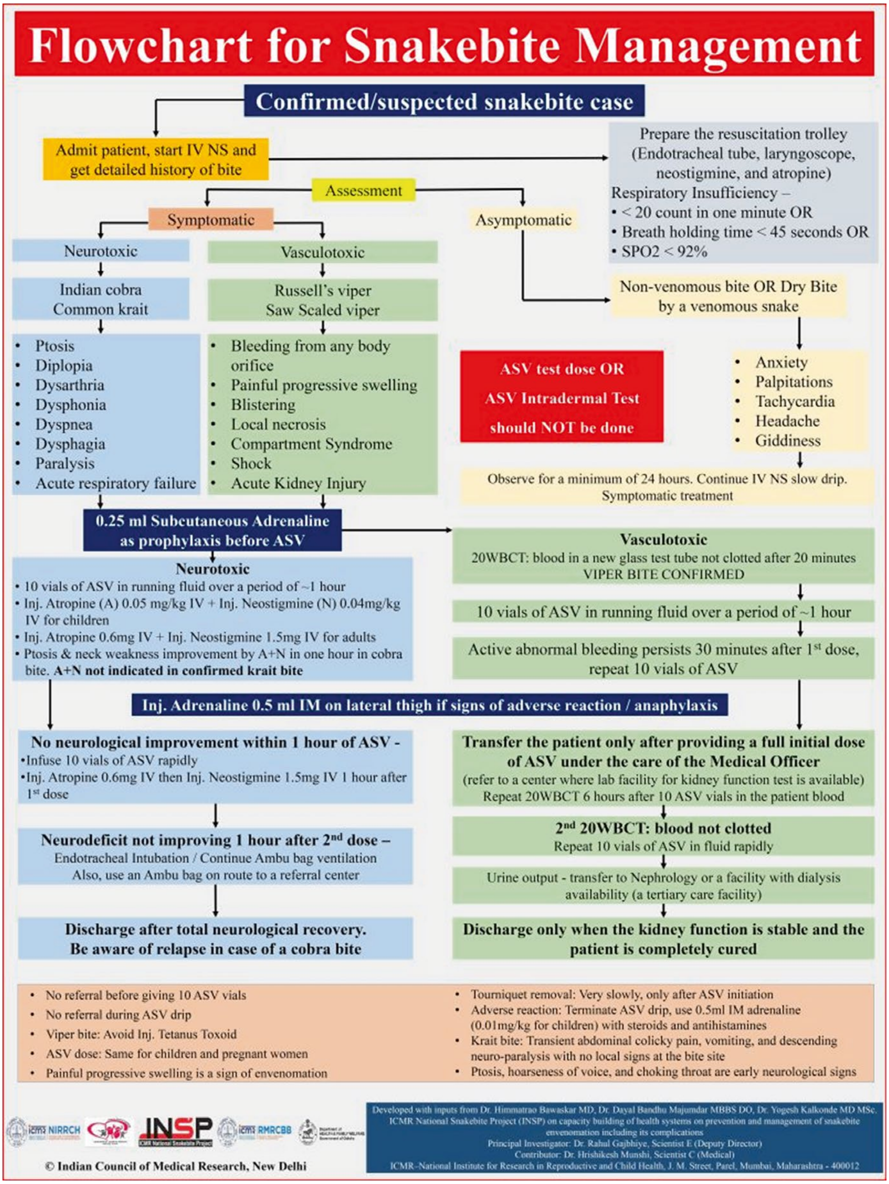
Step 12: Discharge from the ICU

The patient can be discharged from the ICU if the following conditions are present:

- Resolution of paralysis more than 24 h.
- Fifty percent improvement in creatine phosphokinase and potassium.
- Peak expiratory flow rate (PEFR) more than 100 L/min.
- Normal oximetry and blood gas analysis on room air.
- Normalization of BT, CT, CRT, and platelets more than 50,000.
- Stable or improved urine output.
- Most of the snakes are nonvenomous. Some snakebites result in envenomation.

Patients should be informed about late reactions (serum sickness) that can be treated with oral antihistamine or steroid.

A flow chart of the management of snake poisoning is shown in Fig. 19.1.



Flowchart for Snakebite Management

Confirmed/suspected snakebite case

Admit patient, start IV NS and get detailed history of bite

Prepare the resuscitation trolley (Endotracheal tube, laryngoscope, neostigmine, and atropine)
Respiratory Insufficiency –
- < 20 count in one minute OR
- Breath holding time < 45 seconds OR
- SPO2 < 92%

Assessment

Symptomatic

Asymptomatic

Neurotoxic

Indian cobra
Common krait

- Ptosis
- Diplopia
- Dysarthria
- Dysphonia
- Dyspnea
- Dysphagia
- Paralysis
- Acute respiratory failure

Vasculotoxic

Russell's viper
Saw Scaled viper

- Bleeding from any body orifice
- Painful progressive swelling
- Blistering
- Local necrosis
- Compartment Syndrome
- Shock
- Acute Kidney Injury

Non-venomous bite OR Dry Bite by a venomous snake

- Anxiety
- Palpitations
- Tachycardia
- Headache
- Giddiness

Observe for a minimum of 24 hours. Continue IV NS slow drip.
Symptomatic treatment

ASV test dose OR ASV Intradermal Test should NOT be done

0.25 ml Subcutaneous Adrenaline as prophylaxis before ASV

Neurotoxic
- 10 vials of ASV in running fluid over a period of ~1 hour
- Inj. Atropine (A) 0.05 mg/kg IV + Inj. Neostigmine (N) 0.04mg/kg IV for children
- Inj. Atropine 0.6mg IV + Inj. Neostigmine 1.5mg IV for adults
- Ptosis & neck weakness improvement by A+N in one hour in cobra bite. **A+N not indicated in confirmed krait bite**

Vasculotoxic
20WBCT: blood in a new glass test tube not clotted after 20 minutes
VIPER BITE CONFIRMED

10 vials of ASV in running fluid over a period of ~1 hour

Active abnormal bleeding persists 30 minutes after 1st dose, repeat 10 vials of ASV

Inj. Adrenaline 0.5 ml IM on lateral thigh if signs of adverse reaction / anaphylaxis

No neurological improvement within 1 hour of ASV -
- Infuse 10 vials of ASV rapidly
- Inj. Atropine 0.6mg IV then Inj. Neostigmine 1.5mg IV 1 hour after 1st dose

Neurodeficit not improving 1 hour after 2nd dose –
Endotracheal Intubation / Continue Ambu bag ventilation
Also, use an Ambu bag on route to a referral center

Discharge after total neurological recovery.
Be aware of relapse in case of a cobra bite

Transfer the patient only after providing a full initial dose of ASV under the care of the Medical Officer
(refer to a center where lab facility for kidney function test is available)
Repeat 20WBCT 6 hours after 10 ASV vials in the patient blood

2nd 20WBCT: blood not clotted
Repeat 10 vials of ASV in fluid rapidly

Urine output - transfer to Nephrology or a facility with dialysis availability (a tertiary care facility)

Discharge only when the kidney function is stable and the patient is completely cured

- No referral before giving 10 ASV vials
- No referral during ASV drip
- Viper bite: Avoid Inj. Tetanus Toxoid
- ASV dose: Same for children and pregnant women
- Painful progressive swelling is a sign of envenomation

- Tourniquet removal: Very slowly, only after ASV initiation
- Adverse reaction: Terminate ASV drip, use 0.5ml IM adrenaline (0.01mg/kg for children) with steroids and antihistamines
- Krait bite: Transient abdominal colicky pain, vomiting, and descending neuro-paralysis with no local signs at the bite site
- Ptosis, hoarseness of voice, and choking throat are early neurological signs

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Developed with inputs from Dr. Himmatrao Bawaskar MD, Dr. Dayal Bandhu Majumdar MBBS DO, Dr. Yogesh Kalkonde MD MSc.
ICMR National Snakebite Project (INSP) on capacity building of health systems on prevention and management of snakebite envenomation including its complications
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Fig. 19.1 Flowchart for snakebite management

Suggested Reading

Aggarwal R, Aggarwal AN, Gupta D, et al. Low dose of snake antivenom is as effective as high dose in patients with severe neurotoxic snake envenoming. Emerg Med J. 2005;22:397–9. *The article clearly demonstrates no advantage of high-dose antivenom therapy*

Kumar V, Malik R, Chaudhary D, et al. Analytical study involving neuroparalytic envenomation cases reported to a north Indian tertiary care hospital. J Indian Soc Toxicol. 2016;12:2. *PROTOCOL FOR INITIAL MANAGEMENT OF SNAKEBITE. AT HEALTH FACILITIES (PHC/CHC). Snake Bite Prevention and Control, NEDC, DGHS, MOHFW, GoI*

Naphade RW, Shetti RN. Use of neostigmine after snake bite. Br J Anaesth. 1997;49:1065–8. *This article gives an overview of neostigmine in the management of neuroparalytic snake envenomation*

WHO guidelines for the management of snake bite, 2nd edition, 2016.

Part V

Obstetrics

Acute Respiratory Failure During Pregnancy

20

Rajesh Chawla, Prashant Nasa, and Aakanksha Chawla

Case Vignette

A 25-year-old woman at36 weeks of pregnancy was admitted to the hospital with complaints of breathlessness, right-sided chest pain, and swelling of the left leg for 3–4 days. Her body mass index was 40 kg/m^2. She was tachypneic, her chest was clear, and SpO_2 on room air was 90%.

Acute respiratory failure during pregnancy can occur due to many disorders. It can result in significant maternal and fetal morbidity and mortality.

Step 1: Initiate Assessment and Resuscitation

Airway

- Airway evaluation and management remain the priority in the initial resuscitation as in nonpregnant patients.
- Definitive airway (tracheal intubation) is needed in persistent hypoxemia, airway obstruction, impaired laryngeal reflexes, or in altered consciousness.

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- Difficult airway equipment for airway management must be thoroughly checked before proceeding to intubation, and an alternative plan for a definitive airway including surgical access should be identified.
- Intubation should be performed by a senior intensivist/anesthesiologist, especially in the later part of pregnancy, due to upper airway edema, narrow airway caliber, and rapid desaturation due to low functional residual capacity.

Breathing

- Respiratory distress is the most common symptom, but confusion, somnolence, agitation, diaphoresis, and impending respiratory arrest can also be present.
- Supplemental oxygen may be required in some patients depending on their oxygen saturation.
- High-flow nasal oxygenation or noninvasive ventilation (NIV) can be tried only in the controlled ICU setting. Signs of NIV failure and the requirement for intubation should also be identified sooner rather than later. These include increased breathing work, mental status deterioration, hemodynamic instability, and an inability to protect the airway or manage secretions.

Always target SpO_2 of more than 95%. For adequate fetal oxygenation, a maternal arterial oxygen tension (PaO_2) of more than 70 mmHg is required, which corresponds to an oxyhemoglobin saturation of 95%. In pregnant patients, the normal range for paCO2 is typically 30–32 mm Hg. Therefore, when managing a mechanically ventilated pregnant patient, this range is used as the target. A paCO2 level of 40 mm Hg is considered abnormal in this context and indicates respiratory failure.

Circulation

- Two large-bore intravenous cannula (14G or 16G) should be placed to administer fluids.
- Administrate fluid judiciously to optimize preload and at the same time to avoid overload.
- Maintain high cardiac output.
- Nursing in the left lateral (30° wedge to the right hip) position is needed to prevent supine hypotension syndrome.

Step 2: Take History and Physical Examination

- Take detailed history of pregnancy, antenatal evaluation and immunization, respiratory disease (e.g., asthma and tuberculosis), and family history of active respiratory infections.

- A detailed history of respiratory symptoms such as dyspnea, cough, expectoration, and chest pain should be evaluated.
- The physical examination includes an assessment of the severity of respiratory failure by general assessment, respiratory rate, use of accessory respiratory muscles, and signs of impending respiratory arrest (e.g., fatigue, drowsy, silent chest, and bradycardia).
- Assessment of the fetus is also important. Fetal heart sounds and their variability—to ascertain fetal well-being should be assessed along with the maternal assessment.

Step 3: Understand Physiological Changes in Pregnancy

- Pregnancy causes various mechanical, immunological, biochemical, and hemodynamic changes in the cardiorespiratory system (Table 20.1).
- Normal $PaCO_2$ on ABG should be interpreted as a sign of impending respiratory failure as there is a mild respiratory alkalosis in pregnancy (see Table 20.1).
- Inability to maintain a PaO_2 of more than 70 mmHg, or a SaO_2 of more than 95%, with conservative therapy should also be interpreted as a sign of respiratory compromise.

Table 20.1 Effects of pregnancy on pulmonary physiology

	Anatomical changes	Physiological alterations
Airway	Edema, mucosal friability, nasal congestion	Increased respiratory drive
		Hyperventilation
Thorax including lung parenchyma	Widened diameters, widened subcostal angle, elevated diaphragm	Reduced functional residual capacity
		Increased tidal volume, respiratory rate unchanged
		Preserved vital capacity
		Respiratory alkalosis
		Normal oxygenation
Abdomen	Enlarged uterus	Reduced chest wall compliance
Cardiovascular system	Increased left ventricular (LV) mass	Increased cardiac output
	Increased blood volume	
Arterial blood gas		7.40–7.45 pH
		28–32 mmHg $PaCO_2$
		106–110 mmHg PaO_2

Step 4: Send Investigations

- Complete hemogram.
- Liver function tests.
- Renal function tests and serum electrolytes.
- Arterial blood gas.
- Coagulation profile [prothrombin time (PT), INR, activated partial thromboplastin time (aPTT), and fibrinogen].
- When appropriate, send sputum examination/tracheal secretions—Gram stain and aerobic culture sensitivity, throat swab for viral panel including H1N1
- Paired percutaneous blood cultures.
- Additional tests if indicated—D-dimer does not help in pregnancy.
- Chest X-ray with proper shielding.
- Multidetector computed tomographic (MDCT) pulmonary angiography if clinical situation demands.
- Ultrasonography is used to assess the status of the fetus, to evaluate growth, and in suspected case to evaluate deep venous thrombosis.
- Transthoracic echocardiography.

Step 5: Make a Diagnosis of Respiratory Failure in Pregnancy

The various causes of acute respiratory failure are summarized in Table 20.2.

A. *ARDS*
  - The criteria for diagnosis of ARDS are like nonpregnant women (see Chap. 5, Vol. 1).
  - The pregnant state is associated with higher risk of ARDS from both pregnancy-associated and other conditions. The proposed mechanisms of ARDS in pregnancy are increased circulating blood volume, capillary

Table 20.2 Differential diagnosis of acute respiratory failure during pregnancy

Conditions unique to pregnancy	Conditions can be affected by pregnancy	Conditions unaffected by pregnancy
Peripartum cardiomyopathy	Acute pulmonary edema	ARDS
		Bacterial pneumonia
Amniotic fluid embolism Venous air embolism	Aspiration of gastric contents	Fat embolism
Tocolytic therapy-induced acute pulmonary edema	Asthma	Inhalational injury
Severe pre-eclampsia	Venous thromboembolism	
Chorioamnionitis, endometritis	Bacterial and viral pneumonia	Sepsis, trauma, burns
Ovarian hyperstimulation syndrome (OHSS)	Malaria, fungal infections	Acute pancreatitis, transfusion-related acute lung injury (TRALI)

hyperpermeability, hypoalbuminemia, and may be upregulation of acute inflammatory response.

B. *Asthma in pregnancy*
  - Rule of thirds—one-third of patients with asthma in pregnancy improve, and one-third shows no change. One-third worsens and can present in acute severe asthma.
  - The risk of severe asthma exacerbation tends to revert by 3 months' postpartum like nonpregnant. The risk of asthma exacerbation is generally the same during successive pregnancies.

C. *Pulmonary embolism in pregnancy*
  - Pregnancy itself is a hypercoagulable state and an independent risk factor for pulmonary embolism (PE). The risk of PE is increased 5–6 times during pregnancy.
  - Clinical prediction models that are used to predict pretest probability of PE have not been validated in pregnant patients.
  - D-dimers should not be used in pregnant as false-positive rates are high.
  - The initial diagnostic test for venous thrombosis in pregnancy should be duplex ultrasonography if suspicion of DVT or PE is present.
  - Radiographic imaging remains the primary testing modality for diagnosing PE, and it should not be delayed because of concerns about radiation exposure.
  - The diagnosis of pulmonary embolism in pregnant women can utilize ventilation-perfusion (V/Q) scanning or CT pulmonary angiography.

The exposure of radiation to the fetus is the same for V/Q scan or CT pulmonary angiography. However, risk of radiation to pregnant women's breasts is higher with CT angiography. So, V/QScan is preferred in patients with normal X-ray. The ventilation portion of the study can be avoided if perfusion is normal. An algorithm for diagnosis of PE is mentioned in Fig. 20.1.

- Compression ultrasonography and transthoracic echocardiography (TTE) can be used for provisional diagnosis in case of unstable patient with suspected PE.

D. *Ovarian hyperstimulation syndrome (OHSS)*
  - Gestation of 3–8 weeks.
  - Increased vascular permeability—fluid shift from the intravascular to extravascular space—causing pleural or pericardial effusions, ascites, electrolyte imbalances, dyspnea, oliguria, severely enlarged polycystic ovaries, hemoconcentration, and hypercoagulability, electrolyte imbalance are the common presentations.
  - The common criteria for severe and life-threatening OHSS are described in Table 20.3.

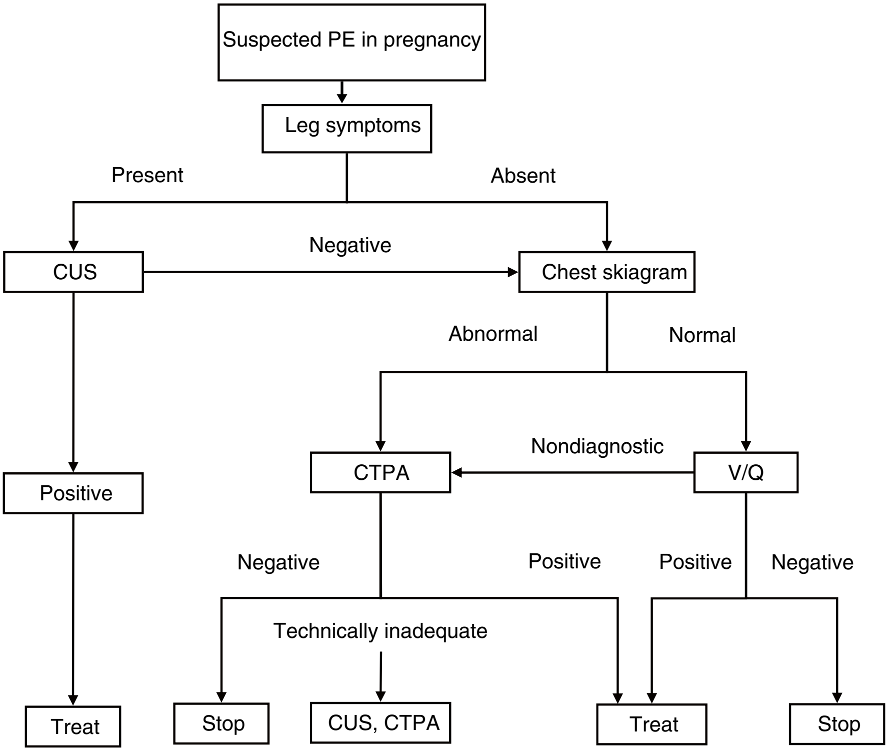
Suspected PE in pregnancy
Leg symptoms
Present
Absent
CUS
Negative
Chest skiagram
Abnormal
Normal
CTPA
Nondiagnostic
V/Q
Positive
Negative
Positive
Positive
Negative
Technically inadequate
Treat
Stop
CUS, CTPA
Treat
Stop

Fig. 20.1 Algorithm for the diagnosis of pulmonary embolism in pregnancy

Table 20.3 Criteria that define the severe and life-threatening stages of OHSS

Severe OHSS	Life-threatening OHSS
Variably enlarged ovary	Variably enlarged ovary
Massive ascites with or without hydrothorax	Tense ascites with or without hydrothorax
Hematocrit >45%	Hematocrit >55%
WBC count >15,000	WBC count >25,000
Oliguria	Oliguria
Creatinine level 1.0–1.5 mg/dL	Creatinine level ≥ 1.6 mg/dL
Creatinine clearance ≥50 mL/min	Creatinine clearance <50 mL/min
Liver dysfunction	Liver failure
Anasarca	Thromboembolic phenomena
	ARDS

E. *Peripartum cardiomyopathy (PPCM)*

The cause of the disease remains unknown.

- The associated conditions include hypertension, pre-eclampsia, multiparity, multiple gestations, and older maternal age.

Table 20.4 Clinical criteria for the diagnosis of PPCM

Development of cardiac failure in the last month of pregnancy or within 5 months postpartum
Absence of another identifiable cause for the cardiac failure
Absence of recognizable heart disease before the last month of pregnancy
LV systolic dysfunction shown by echocardiographic data such as depressed shortening fraction (e.g., ejection fraction less than 45%, M-mode fractional shortening less than 30%, or both, and an LV end-diastolic dimension of more than 2.7 cm/m^2)

- Signs and symptoms are paroxysmal nocturnal dyspnea, chest pain, nocturnal cough, new regurgitant murmurs, pulmonary crackles, increased jugular venous pressure, and hepatomegaly.
- Identify other cardiac and noncardiac disorders such as coronary, rheumatic, or valvular heart disease; arrhythmias; and family history of cardiomyopathy or sudden death and other risk factors of cardiac diseases such as hypertension (chronic, gestational, pre-eclampsia), diabetes, dyslipidemia, thyroid disease, anemia, prior chemotherapy or mediastinal radiation, sleep disorders, current or past alcohol or drug abuse, and collagen vascular disease.
- The diagnosis of PPCM is a diagnosis of exclusion and should be made when other possible causes of acute/subacute heart failure have been ruled out (Table 20.4).

F. *Tocolytic-induced pulmonary edema*

Terbutaline (beta 2 agonist) use to inhibit preterm labor may induce pulmonary edema. This is more commonly seen in pregnancy with multiple gestations. It is also seen sometimes with magnesium sulfate infusion.

Exclude other causes of cardiogenic or non-cardiogenic causes of pulmonary edema.

Give supplemental oxygen, fluid restriction, and diuresis.

Most cases resolve within 24 hours.

Step 6: Treat the Specific Cause

The general management of respiratory failure in pregnancy is similar to the management in nonpregnant women, although one should be careful about normal physiologic alterations that occur in the parturient state and effect of ventilator strategies.

A. *Management of ARDS and mechanical ventilation in pregnant patients*

- Lung-protective strategy to avoid volutrauma, biotrauma, atelectrauma, leading to less ventilator-induced lung injury has been found to reduce mortality and improve outcome in patients with ARDS.

  Lung-protective strategy causes hypoventilation, which is tolerated to maintain (permissive hypercapnia) the pH between 7.25 and 7.35. This strategy has not been assessed in pregnancy. If necessary, in case of severe ARDS, mild hypercapnia with $PaCO_{2\ \text{should be}}$ maintained less than 40 mmHg.

- Permissive hypercapnia can cause fetal acidosis, an increase in intracranial pressure, and a right shift in the hemoglobin dissociation curve and in the first 72 h may lead to retinopathy of prematurity, so lung-protective ventilatory strategy in pregnant patients should be used with close monitoring of the fetal status with the biophysical profile.
- Oxygen levels should be closely monitored in pregnancy and kept higher than in nonpregnant women (preferably $SpO_2 \geq 95\%$) and pO_2 above 70 mm Hg.
- Target a $paCO_2$ between 30 and 32 mmHg for proper fetal gas exchange.
- Chest wall compliance is reduced by the enlarging uterus, and the usual pressure limits (e.g., plateau pressure of 35 cmH_2O) may not be appropriate. This may lead to increase need of higher airway pressures (without increased trans-pulmonary pressure) for appropriate tidal volumes in pregnant women, especially in the last trimester.
- Hyperventilation and alkalosis should be avoided to prevent uterine vasoconstriction.
- The indication for prone position ventilation is the same as the general population with special care for gravid uterus with adequate padding.

B. *Management of asthma in pregnancy*

- Management of asthma in pregnancy is similar to nonpregnant women.
- Beta-agonist bronchodilators with or without ipratropium are given with spacer and metered dose inhaler or in nebulizations.
- IV corticosteroids are the mainstay of the treatment in severe asthma exacerbation like in a normal adult.

C. *PE during pregnancy*

- Acute treatment of PE can be done with low-molecular-weight heparin (LMWH) or unfractionated heparin (UFH) and should be started without delay whenever PE is suspected or confirmed.

LMWH is first-line therapy for the treatment of acute PE in the general population and in pregnancy and is associated with fewer adverse effects than unfractionated heparin.

- Thrombolysis can have obstetric and neonatal complications such as pregnancy loss, abruption, and preterm labor. However, complications have been found no more than nonpregnant. Therefore, the use of thrombolytics in pregnancy should be reserved for women with PE who are hemodynamically unstable or with refractory hypoxemia.
- The anticoagulation is continued for 6 weeks in postpartum or total duration of minimum three months, whichever is later.
- Warfarin and direct oral anticoagulants are usually avoided in pregnancy. Warfarin crosses the placenta and associated with fetal nasal, ophthalmologic, or central nervous system abnormalities.

Heparins are thus the mainstay treatment during the entire period of pregnancy. Start oral anticoagulants only after delivery.

D. *OHSS*

- Syndrome is self-limiting, and resolution parallels the decline in serum HCG levels: 7 days in nonpregnant patients and 10–20 days in pregnant patients.

- Monitor frequently for deterioration with physical examinations, daily weights, and periodic laboratory measurements of complete blood counts, electrolytes, and analysis of renal and hepatic function.
- Severe disease—placement of two large-bore peripheral intravenous catheters or a central venous catheter (preferred) for fluid management may be required.
- Use the Foley's catheter for close monitoring of the urine output.
- Normal saline with or without glucose is the crystalloid of choice, and potassium-containing fluids should be avoided because patients with OHSS could develop hyperkalemia.
- In more severe cases with significant hypovolemia, hemoconcentration (hematocrit >45%), hypoalbuminemia (serum albumin level < 3.0 g/dL), or severe ascites, albumin can be given as a plasma expander along with diuretics (furosemide) once hematocrit is 36–38%.
- If respiratory symptoms worsen, thoracentesis/paracentesis should be performed.
- If ARDS develops and mechanical ventilation is required, lung-protective strategies must be used.

E. *PPCM*

- Diuretic agents, including loop diuretics, and nitrates are initial agents for symptom relief, in most patients because they cause symptomatic relief of pulmonary and peripheral edema.
- Angiotensin-converting enzyme inhibitor or angiotensin receptor blockers are contraindicated before delivery and can be used only in postpartum females.
- Hydralazine and nitrates are the vasodilators of choice for pregnant women.
- β-Blockers (sustained-release metoprolol succinate, carvedilol, and bisoprolol) have been shown to reduce mortality with current or prior heart failure and reduced ejection fraction and therefore constitute the first-line therapy for all stable patients unless contraindicated (Table 20.5).

Table 20.5 Treatment of PPCM

Nonpharmacological measures	Drugs for routine use	In selected patients	Therapies avoided
Hypertension control (salt restriction)	Diuretics	Aldosterone antagonists	Angiotensin-converting enzyme inhibitors
Fluid restriction	β-Blockers	Inotropes	Angiotensin receptor blockers
	Digoxin	Anticoagulation	Many antiarrhythmic drugs
	Vasodilators	Implantable defibrillators	Nonsteroidal anti-inflammatory drugs
		Biventricular pacing	Nondihydropyridine calcium channel blockers
		Cardiac transplantation	

- Digoxin if required is safe in pregnancy with the same level of monitoring as in nonpregnant.
- Anticoagulation to prevent systemic thromboembolism is recommended in all females till resolution of cardiomyopathy or 3 months postpartum, whichever is earlier.

Suggested Reading

Arany Z, Elkayam U. Peripartum cardiomyopathy. Circulation. 2016;133(14):1397–409. *This article discusses the updated pathogenesis, risk factors, diagnosis, management, and prognosis of the peripartum cardiomyopathy*

Avecillas JF, Falcone T, Arroliga AC. Ovarian hyperstimulation syndrome. Crit Care Clin. 2004;20:679–95. *This article reviews the management of OHSS*

Bhatia PK, Biyani G, Mohammed S, Sethi P, Bihani P. Acute respiratory failure and mechanical ventilation in pregnant patient: a narrative review of literature. J Anaesthesiol Clin Pharmacol. 2016;32(4):431–9. *This article focuses on developments related to ALI and ARDS and reviews epidemiology, pathogenesis, and therapeutic advances during pregnancy*

Global Strategy for Asthma Management and Prevention, Global Initiative for Asthma (GINA). www.ginasthma.org. 2024. *A comprehensive guideline for the management of asthma in adults*

Lapinsky SE. Acute respiratory failure in pregnancy. Obstet Med. 2015;8(3):126–32. *This article addresses the group of pregnant women with symptomatic asthma as well as those whose asthma is asymptomatic as a result of good control*

Lapinsky SE. Management of acute respiratory failure in pregnancy. Semin Respir Crit Care Med. 2017;38(2):201–7. *This review focuses on the clinical manifestations and management issues of the most common causes of respiratory failure during pregnancy*

Munnur U, Bandi V, Guntupalli KK. Management principles of the critically ill obstetric patient. Clin Chest Med. 2011;32:53–60. *The article reviews the management of common serious problems such as hypertensive disorders, sepsis, and hemorrhage in pregnant patients*

Severe Preeclampsia

21

Rajesh Chawla, Prashant Nasa, Renu Chawla,
and Bharat G. Jagiasi

Case Vignette

A 23-year-old female at 30 weeks of pregnancy was admitted to the hospital with an episode of seizure, epigastric pain, and decreased urine output. She had pedal edema, and her blood pressure (BP) on admission was 190/110 mmHg. Her urine output was 300 mL in the past 24 h. Urine examination showed protein 4+ and hemoglobin 8 g%. Liver function test showed elevated aspartate aminotransferase and alanine aminotransferase.

Hypertensive disorders (preeclampsia, chronic hypertension, preeclampsia superimposed on chronic hypertension, and gestational hypertension) complicate 5–10% of all pregnancies. Preeclampsia either alone or superimposed on chronic hypertension may be associated with adverse outcomes.

Preeclampsia is a multi-system organ disorder characterized by the new onset hypertension (systolic blood pressure > 140 mmHg or diastolic blood pressure more than 90 mmHg on at least two occasions at least four hours apart) presenting after

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20 weeks of gestation or postpartum with significant proteinuria or the new onset hypertension and end-organ dysfunction with or without proteinuria.

Most patients (90%) are diagnosed at or after 34 weeks of gestation and progress until delivery or postpartum but some may develop earlier (10%) and be associated with higher maternal and perinatal complications. Delivery of the placenta usually results in the resolution of maternal organ dysfunction and results in normotension.

Step 1: Initial Assessment and Resuscitation

- Always anticipate difficult airways in pregnant patients (Table 21.1).
- Endotracheal intubation should be performed by a senior intensivist/anesthesiologist.
- Difficult airway equipment for airway management must be thoroughly checked before proceeding to intubation, and alternative plans for definitive airway including surgical access should already be identified.
- Supplemental oxygen may be required in some patients depending on their oxygen saturation.
- Target SpO_2 of more than 95% with oxygen or ventilation.

Circulation

- Two large-bore intravenous cannulas (14G or 16G) should be placed to administer fluids.
- Radial arterial catheter is preferred in patients with severe preeclampsia as blood pressure is labile and changes rapidly with the administration of vasoactive medications (like labetalol), labor, or anesthetic interventions.
- The Foley catheter should be placed to monitor urine output.
- Judicious fluid administration is needed to optimize preload and at the same time to avoid overload.
- Nurse in the left lateral position (30° wedge to the right hip) to prevent supine hypotension syndrome.
- Treatment of blood pressure with careful monitoring and target blood pressure is close to the baseline, rather than normal, to preserve uteroplacental perfusion while monitoring the fetus and ensuring late decelerations do not develop.

Table 21.1 Risk factors for difficult airway during pregnancy

Progesterone-induced airway edema is further exacerbated in pregnancy-induced hypertension (PIH), which needs a smaller endotracheal tube and increases the risk of bleeding during airway instrumentation.
Thick neck, large breasts
Increased risk of hypoxemia—decreased cardiopulmonary reserve and increased metabolic requirements
Increased risk of aspiration of gastric contents

Disability (Neurological)

- Magnesium is indicated in all patients with severe preeclampsia for intrapartum and postpartum seizure prophylaxis.
- Magnesium sulfate is a drug of choice for the control of seizures.
- This can be given as 4 g diluted in 20 mL of IV fluid bolus over 10 min followed by 5 g intramuscularly in each buttock.
- See Step 6 Seizure control.

Step 2: Take History and Physical Examination and Make a Diagnosis

- A detailed history should be taken of previous pregnancy, antenatal evaluation, immunization, hypertension, pregestational diabetes, and PIH (pregnancy-induced hypertension) in the last pregnancy.
- Complications and outcomes of the previous pregnancy and family history of hypertension should be required.
- History includes symptoms displaying end-organ effects to detect the presence of severe preeclampsia:
  - Headache
  - Visual disturbances—blurred, scintillating scotomas
  - Altered mental status
  - Blindness
  - Dyspnea
  - Edema
  - Epigastric or right upper quadrant abdominal pain
  - Weakness or malaise—may be evidence of hemolytic anemia
- The physical examination includes the evaluation of end-organ dysfunction for diagnosis of severe preeclampsia:
  - Altered mental status
  - Decreased vision or scotomas
  - Papilledema
  - Epigastric or right upper quadrant abdominal tenderness
  - Peripheral edema
  - Seizures
  - Focal neurologic deficit
- PIH (preeclampsia) is defined as the presence of hypertension (BP $\geq$ 140/90 mmHg) on two occasions, at least 4 h apart in more than 20 weeks of gestation in women with previously normal BP and who have proteinuria ($\geq$0.3 g protein in 24-h urine specimen or urinary protein: creatinine ratio is greater than 30 mg/mmol), with or without pedal edema, or the new onset of hypertension and significant end-organ dysfunction with or without proteinuria.
- Severe preeclampsia is defined in Table 21.2.

Table 21.2 Criteria for diagnosing severe preeclampsia

Systolic blood pressure $\geq$ 140 mmHg or diastolic blood pressure $\geq$ 90 mmHg on at least two occasions at least four hours apart after 20 weeks of gestation in a previously normotensive patient AND the new onset of one or more of the following
Proteinuria $\geq$0.3 g in a 24-hour urine specimen or protein/creatinine ratio $\geq$ 0.3 (mg/mg) (30 mg/mmol) in a random urine specimen or dipstick $\geq$2+ if a quantitative measurement is unavailable
Platelet count <100,000/microL
Serum creatinine >1.1 mg/dL (97.2micromol/L) and/or doubling of the creatinine concentration in the absence of other renal diseases
Liver transaminases at least twice the upper limit of the normal concentrations for the local laboratory and/or severe persistent right upper quadrant or epigastric pain unresponsive to medication
Pulmonary edema
Cerebral or visual symptoms (e.g., new-onset and persistent headaches not accounted for by alternative diagnoses and not responding to usual doses of analgesics; blurred vision, flashing lights or sparks, or scotomata)
If systolic blood pressure is $\geq$160 mmHg or diastolic blood pressure is $\geq$110 mmHg, confirmation within minutes is sufficient.

Adapted from: American College of Obstetricians and Gynecologist (ACOG) Practice Bulletin No. 222: Gestational Hypertension and Preeclampsia. Obstet Gynecol 2022; 135:e1–e237.

Criteria for superimposed preeclampsia: In a woman with chronic/preexisting hypertension are a new onset of proteinuria, significant end-organ dysfunction, or both after 20 weeks of gestation.

- Eclampsia is defined as seizures that cannot be attributable to other causes in a woman with preeclampsia.

Step 3: Send investigations

- Complete blood cell count.
- Liver function tests.
- Renal function tests and serum electrolytes.
- Arterial blood gas and blood glucose.
- Coagulation profile (prothrombin time [PT], activated partial thromboplastin time [aPTT], and fibrinogen, international normalized ratio).
- Lactate dehydrogenase.
- Serum uric acid.
- Urine routine microscopy, 24-h urine protein, and creatinine, and urinary protein:creatinine ratio.
- Additional tests—peripheral smear, serum magnesium levels.
- Ultrasonography is used to assess the status of the fetus as well as to evaluate growth retardation.
- Fetal monitoring.
- Transthoracic echocardiography.

- Patients with thrombocytopenia and hemolysis, neurological findings, and normal coagulation function should be assessed for ADAMTS13 activity to exclude thrombotic thrombocytopenic purpura.

Step 4: Make a Differential Diagnosis (Table 21.3)

Principal differentiation includes exacerbation of underlying preexisting renal disease, acute fatty liver of pregnancy, thrombotic microangiopathy (TTP or HUS), and exacerbation of systemic lupus.

The various conditions that can cause acute hepatic failure in pregnancy should be considered before making a diagnosis of severe preeclampsia–eclampsia (Table 21.4).

Table 21.3 Differential diagnosis

Severe preeclampsia (abdominal pain)
Abruptio placentae
Abdominal aneurysm
Acute appendicitis
Blunt abdominal trauma
Cholecystitis and biliary colic
Ovarian torsion
Thrombotic thrombocytopenic purpura
Poisoning
Eclampsia (seizure)
Cerebrovascular accidents
Brain tumors
Brain infections—meningitis, encephalitis, abscesses
Thrombotic thrombocytopenic purpura
Metabolic disorders
Hypertensive encephalopathy
Illicit drug use
Postdural puncture syndrome
Epilepsy/status epilepticus
Posterior reversible encephalopathy syndrome

Table 21.4 Comparison of severe preeclampsia–eclampsia, intrahepatic cholestasis of pregnancy, HELLP syndrome, and AFLP

	Severe preeclampsia–eclampsia	Intrahepatic cholestasis of pregnancy	HELLP syndrome	AFLP
Trimester	Second to third	Second to third	Third	Third
Incidence (%)	1–5	0.1	0.2–0.6	0.005–0.01
Family history	Occasionally	Often	No	Occasionally
Presence of preeclampsia	Yes	No	Yes	50%

(continued)

Table 21.4 (continued)

	Severe preeclampsia–eclampsia	Intrahepatic cholestasis of pregnancy	HELLP syndrome	AFLP
Typical clinical features	Hypertension, edema, proteinuria, neurological deficits (headaches, seizures, coma)	Pruritus, mild jaundice, elevated bile acids	Hemolysis thrombocytopenia (<50,000 often)	Liver failure with coagulopathy, encephalopathy, hypoglycemia, disseminated intravascular coagulation
Aminotransferases	None/mild	Mild to 10- to 20-fold elevation	Mild to 10- to 20-fold elevation	300–500 typical but variable
Bilirubin	Normal— < 5 mg/dL	<5 mg/dL	<5 mg/dL unless massive necrosis	Often <5 mg/dL, higher if severe
Hepatic imaging	Normal—hepatic infarcts	Normal	Hepatic infarcts hematomas, rupture	Fatty infiltration
Histology (usually not performed)	Periportal hemorrhage, necrosis, fibrin deposits	Normal–mild cholestasis, no necrosis	Patchy/extensive necrosis and hemorrhage	Microvesicular fat in zone 3 Subunit, long-chain 3-hydroxy acyl-CoA dehydrogenase defect—yes No fatty acid oxidation defect
Recurrence in subsequent pregnancies	20% risk	60–70%	4–19%	Rare
Termination of pregnancy	Deliver after 36 weeks and early if worsening Preeclampsia	Ursodeoxycholic acid; delivery before 37 weeks	Prompt delivery is essential	Prompt delivery is essential

Step 5: Admit to the ICU and Identify Organ Dysfunctions and Support Them

- ICU admission is indicated with:
  - Eclampsia
  - Hemorrhage
  - Hyperkalemia
  - Severe oliguria
  - Coagulation support
  - Intravenous antihypertensive treatment—initial stabilization of severe hypertension—evidence of cardiac failure

  - Abnormal neurology
  - Placental abruption
  - Severe preeclampsia
  - Hemolysis, elevated liver enzymes, and low platelet (HELLP) syndrome
  - Chorioamnionitis
  - Acute pulmonary edema
  - Respiratory failure
  - Acute respiratory distress syndrome
  - Acute renal failure
  - Maternal monitoring is required with severe preeclampsia:
  - Repeated clinical assessment including neurological examination (deep tendon reflexes for magnesium toxicity)
  - ECG
- Arterial BP—noninvasive BP can be tried initially but may be incorrect with inadequate cuff size
- Pulse oximetry
- Foley catheterization—urine output monitoring
- Blood gas monitoring
- CVP monitoring—infusion of vasopressors
- Additional—intra-abdominal pressure monitoring during resuscitation, serum magnesium levels

Step 6: Management of Severe Preeclampsia

The definitive treatment of preeclampsia is the delivery of the placenta. The timing of delivery depends on gestational age, the severity of preeclampsia, and maternal and fetal conditions.

Another important aspect in the management of severe preeclampsia is the control of hypertension.

A. *BP control*
  - Arterial pressure greater than 160/110 mmHg in preeclampsia can increase the risk of complication, and it should be controlled.
  - BP control should only be done in the ICU, preferably with arterial line monitoring.
  - BP control should also be done along with fetal monitoring. Avoid sudden falls in BP as it can result in fetal distress.
  - The goal of BP control is a 15–25% reduction in the mean arterial pressure, and a reduction of pressure to baseline BP levels (<140/90 mmHg) rather than normal BP, should be avoided as it may compromise placental perfusion.
  - *Drugs*
    - Labetalol (IV 20 mg) can be given initially followed by doubling the dose every 10 min to a cumulative dose of 300 mg. This drug can result in

  severe bradycardia. A continuous infusion of labetalol at a rate of 0.5–2 mg/min can also be used.
  - Hydralazine (5–10 mg) can be given every 20 min (maximum of 40 mg) until BP is controlled.
  - Nifedipine or nicardipine can be given (sudden precipitous decrease in BP or tachycardia can occur).
  - Intravenous nitroglycerin (10–100 mg/min) or sodium nitroprusside (2–8 mg/min) can be given. Prolonged use of nitroglycerin may lead to methemoglobinemia. Cyanide toxicity in the mother and fetus may occur with sodium nitroprusside, limiting its use to less than 4 h and only as a last resort.

B. *Seizure control*
- The initial management of eclampsia includes airway, breathing, and circulation.
- Seizure prophylaxis is given intrapartum or postpartum with magnesium sulfate in cases of severe preeclampsia.
- The initial bolus of magnesium (4 g over 5–15 min) is followed by an infusion of 1–2 g/h maintained for 24 hrs.
- The mechanism of action of magnesium is unknown, but magnesium suppresses excitatory neurotransmitter release by replacing calcium at nerve endings.
- Monitor toxicity—loss of deep tendon reflexes; loss of patellar reflex occurs when the plasma magnesium level is more than 10 mg%. Look for respiratory muscle weakness.
- Magnesium has a relatively narrow therapeutic range, and target magnesium serum concentrations are 5–8 mg/dL.
- Infusion dose should be reduced in cases of renal dysfunction. Serum magnesium levels should be monitored every 4–6 hours and whenever a seizure occurs or signs of toxicity are present, as per Table 21.5.

Table 21.5 Clinical manifestations related to the serum concentration of magnesium

Serum magnesium levels (mg/dL)	Effects
5–8	Therapeutic
8–12	Loss of deep tendon reflexes
12–16	Muscular paralysis and respiratory difficulties
>17	Conduction disturbances
>25	Cardiac arrest

- In recurrent seizures, an additional 2–4 g of magnesium sulfate can be given over 5 mins concurrently with the magnesium sulfate infusion.
- Calcium gluconate 15–30 mL of a 10% solution, administered intravenously over 2–5 minutes, is given to women with cardiac arrest or severe cardiac toxicity related to magnesium toxicity.
- If seizures are not controlled by repeat magnesium bolus, then diazepam or lorazepam can be administered (see Chap. 36, Vol 1).
- Discontinue magnesium sulfate 24 h after delivery.

C. *Fluid management*
  - Despite peripheral edema, patients with preeclampsia are volume-depleted with high peripheral vascular resistance. Diuretics should be avoided.
  - Aggressive volume resuscitation, on the other hand, may lead to pulmonary edema, which is a common cause of maternal morbidity and mortality. Because volume expansion has no demonstrated benefit, patients should be fluid-restricted, when possible, at least until the period of postpartum diuresis.
  - Central venous or pulmonary artery pressure monitoring or other hemodynamic monitoring modalities may be indicated in critical cases.
  - Careful measurement of fluid input and output is advisable, particularly in the immediate postpartum period.

D. Decide the timing and type of *delivery*
  - As maternal morbidity is very high with severe preeclampsia, prompt delivery is indicated regardless of gestational age.
  - Women with severe preeclampsia who are managed expectantly (nonsevere disease) must be delivered under the following circumstances:
    - Severe hypertension develops refractory to treatment
    - Nonreassuring fetal heart status
    - Uncontrollable BP
    - Oligohydramnios, with amniotic fluid index of less than 5 cm
    - Severe intrauterine growth restriction
    - Oliguria (<500 mL/24 h)
    - Serum creatinine level of at least 1.5 mg/dL
    - Pulmonary edema
    - Shortness of breath or chest pain with pulse oximetry of <94% on room air
    - Headache that is persistent and severe
    - Right upper quadrant tenderness with deteriorating liver function test
    - Development of HELLP syndrome
  - Severe hypertension after 34 weeks when their blood pressure has been controlled and a course of corticosteroids has been completed (if appropriate).
  - Offer birth to women with pre-eclampsia before 34 weeks only after discussion with neonatal and anesthetic teams and a course of corticosteroids has been given.
  - Preeclampsia is not an indication for caesarian delivery and many patients can have a normal vaginal delivery.

Step 7: Watch for complications

- Abruptio placentae
- Disseminated intravascular coagulopathy (DIC)
- Renal insufficiency and acute renal failure
- HELLP syndrome
- Eclampsia
- Cerebral hemorrhage
- Fetal changes—intrauterine growth restriction, abruptio placentae, oligohydramnios
- Intrauterine fetal death

Step 8: Managing Complications

HELLP syndrome

- HELLP syndrome can complicate 4–12% of patients with severe preeclampsia.
- Signs and symptoms are right upper quadrant or epigastric pain, nausea and vomiting, malaise, and nonspecific viral-like symptoms. Physical examination findings include right upper quadrant or epigastrium tenderness and generalized edema.

  Tennessee classification:

- Hemolysis: established by the presence of at least two of the following:
- Peripheral smear showing schistocytes and burr cells
- Serum bilirubin ≥1.2 mg/dL
- Low serum haptoglobin (≤25 mg/dL) or LDH ≥2 times the upper level of normal
- Severe anemia unrelated to blood loss
    Elevated liver enzymes
    Aspartate aminotransferase (AST) or alanine aminotransferase (ALT) ≥2 times the upper level of normal
    Low platelets: <100,000 cells/microL
- Delivery is the definitive treatment for HELLP syndrome.
- Delivery is indicated for women with HELLP syndrome at greater than 34 weeks of gestation.
- During labor and for 24-h postpartum, patients should receive intravenous magnesium sulfate for seizure prophylaxis.
- If gestation is less than 34 weeks, delivery may be delayed for 48 hours to administer a steroid course of either betamethasone (12 mg intramuscularly every 24 hours for two doses, with delivery 24 hours after the last dose) or dexamethasone (6 mg intramuscularly every 12 hours for 2 days).
- Platelets are generally transfused when the platelet count is less than 20,000/mm^3. For cesarean delivery or with any significant bleeding, platelets should be transfused if the platelet count is less than 50,000/mm^3.

Acute Pulmonary Edema

- Management is similar to nonpregnant patients.
- Intravenous furosemide (bolus 20–40 mg over 2 min) is used to promote diuresis. The repeated doses of 40–60 mg are given after 30 min or infusion if there is inadequate diuretic response (maximum dose 120 mg/h).
- Careful fetal monitoring, fluid restriction, and strict fluid balance and positioning (such that the head is elevated) are required.

Suggested Reading

Coppage KH, Sibai DM. Treatment of hypertensive complications in pregnancy. Curr Pharm Des. 2005;11:749–57. *The article reviews the management of severe hypertension during pregnancy*

Gestational Hypertension and Preeclampsia: ACOG Practice Bulletin, Number 222. Obstet Gynecol. 2020; 135:e237. Reaffirmed 2023. *Guidelines on management of hypertension and preeclampsia*

Martin JN Jr, Thigpen BD, Moore RC, Rose CH, Cushman J, May W. Stroke and severe preeclampsia and eclampsia: a paradigm shift focusing on systolic blood pressure. Obstet Gynecol. 2005;105:246–54.

Munnur U, Bandi V, Guntupalli KK. Management principles of the critically ill obstetric patient. Clin Chest Med. 2011;32(1):53–60. *This review discusses the principles in the management of critical illness during pregnancy such as peripartum cardiomyopathy, hypertensive crisis, cardiopulmonary resuscitation, and massive transfusion protocol*

NICE (National Institute for Health and Care Excellence) Hypertension in pregnancy. Diagnosis and management. Clinical guideline: Published 25 August 2010. Updated 2018. *This is updated evidence on the management of preeclampsia and severe preeclampsia*

Sibai BM. Diagnosis, controversies, and management of the syndrome of hemolysis, elevated liver enzymes, and low platelet count. Obstet Gynecol. 2004;103:981–91. *This review emphasizes the controversies surrounding the diagnosis and management of the HELLP syndrome and gives recommendations for diagnosis, management, and counseling of these women*

Sibai BM. Imitators of severe preeclampsia. Obstet Gynecol. 2007;109:956–66.

Thomopoulos C, Hitij JB, De Backer T. Management of hypertensive disorders in pregnancy: a Position Statement of the European Society of Hypertension Working Group ‘Hypertension in Women’. J Hypertens. 2024;42(7):1109–32. *Current comprehensive guidelines on hypertensive disorder in pregnancy*

Part VI

Perioperative Care

General Issues in Perioperative Care

22

Prakash Shastri, Vinod K. Singh, and Rahul K. Rajput

Case Vignette

A 25-year-old woman who developed severe post-partum hemorrhage after delivery of a still-born baby was taken up for emergency hysterectomy under general anesthesia with rapid sequence intubation using 150 mg thiopentone, rocuronium 50 mg, fentanyl 50 mcg, 7.5 mm tracheal tube, and controlled ventilation with FiO_2 of 1.0 and 0.8 MAC sevoflurane. During the procedure, the patient was administered 3 units of whole blood, 1 unit of FFP, and 2 liters of Ringer's lactate solution. Dopamine infusion was used to maintain the mean blood pressure around 70 mmHg. At the end of the procedure, the patient was transferred to the ICU without reversal of neuromuscular blockade. In the ICU, the patient was mechanically ventilated and the dopamine was tapered off. The patient was hypothermic and anuric, with a hemoglobin of 6.5 g/dl, platelet count of 37000/mm^3, INR of 5.1, urea of 50 mg/dl, creatinine of 2.7 mg/dl, and raised liver enzymes. ECG showed tall T waves and a blood gas analysis showed serum potassium of 6.1. Corrective measures for hyperkalemia were instituted and the patient was allowed to rewarm. After overnight ventilation and one episode of hemodialysis, the patient was extubated. Hemodialysis continued for another two days until the patient's urine output improved.

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Perioperative medicine is a multidisciplinary, patient-centered system aimed at improving surgical outcomes and reducing complications by providing continuous care from the indication for surgery until full recovery. The risk of perioperative adverse events depends on the patient's disease condition before surgery, the prevalence of comorbidities, the urgency of the operation, and the magnitude, type, and duration of the surgical procedure. The usual principles of coordinated evidence-based resuscitation, monitoring, nursing, and medical care are applicable to these patients as well. There are, in addition, a number of special circumstances that operate in these patients. This chapter attempts to summarize these principles and factors.

Step 1: Assess the Reason for Perioperative Admission to the ICU

(a) Patient Factors
  - Comorbidities: Patients with pre-existing conditions (e.g., heart disease, respiratory failure, diabetes) often require closer monitoring and management.
  - Age: Older patients may have higher risks for complications and may benefit from intensive care support.
  - Functional Status: Patients with limited functional capacity or poor performance status and frailty may need ICU admission for better postoperative care.

(b) Surgical Factors
  - Type of Surgery: Major surgeries (e.g., cardiac, thoracic, complex abdominal procedures) typically carry higher risks and may require ICU admission.
  - Duration of Surgery: Prolonged procedures increase the likelihood of complications, warranting closer monitoring.
  - Intraoperative Complications: Any complications that arise during surgery (e.g., significant blood loss, need for blood products) may necessitate ICU care.

(c) Anesthetic Factors
  - Type of Anesthesia: Certain anesthetic techniques or agents may require postoperative monitoring in an ICU setting, especially those that impact respiratory or cardiovascular function.
  - Emergent or Urgent Procedures: Unplanned surgeries, particularly in unstable patients, often require intensive care support postoperatively.

(d) Postoperative Considerations
  - Need for Close Monitoring: Patients who are at high risk for respiratory distress, hemodynamic instability, or other complications may be admitted to the ICU for enhanced monitoring.
  - Ventilation Support: Patients requiring mechanical ventilation or significant respiratory support postoperatively typically need ICU care.

- Fluid and Electrolyte Management: Those needing careful management of fluids, electrolytes, or renal function may benefit from ICU admission.

(e) Clinical Judgment

Multidisciplinary Assessment: Input from surgeons, anesthesiologists, and intensivists is crucial in determining the need for ICU admission based on the overall clinical picture.

- Initial resuscitation, monitoring, investigations, and continuing care differ in each of these scenarios.
- Attempts have been made to predict the risk of ICU admission after surgery. It has been identified that intraoperative vasopressor requirements (adrenaline, noradrenaline, and vasopressin), as well as the need for vasopressors at the end of surgery and emergency surgery, are good predictors of ICU admission.

Step 2: Obtain a Structured Handover from the Anesthesia and Surgical Teams. Take Focused History, Perform Physical Examination and Relevant Investigations

- Confirm the patient's identification.
- Intraoperative findings and surgical procedures performed.
- Duration of surgery.
- Anesthesia chart and postoperative notes: pay attention to any airway problems encountered, placement of venous and arterial lines, and all monitoring devices.
- Intraoperative complications, estimated blood loss, transfusions of blood and blood products, and the nature and volume of other fluids administered.
- Postoperative instructions.
- Placement of surgical drains and current drainage.
- Urinary catheter and output.
- Fluids, antibiotics, analgesia, antiemetic prescription.
- Epidural catheters or patient-controlled analgesia (PCA) pumps.
- Review of the medical records of the patient for comorbid conditions.
- Drug history—aspirin, other antiplatelet agents, oral anticoagulants, and oral hypoglycemic agents.
- Postoperative laboratory, imaging, and electrocardiogram studies should be selected on a case-by-case basis.

Step 3: Identify Problems of Immediate Concern

(a) Hemodynamic instability

- Intraoperative blood loss, inadequate resuscitation, vasopressor infusions, transport.
- Assess patient volume status using clinical signs and noninvasive techniques such as IVC collapsibility on ultrasound examination. Decide whether intravenous fluid is required and administer it in a titrated fashion.

- The cardiovascular examination is primarily directed at the assessment of adequate clinical perfusion. Impressions from the initial survey of clinical perfusion plus any available data from invasive monitoring can be used to assess appropriate hourly maintenance fluid rate and the need for further volume resuscitation.
- Titrate any vasopressors.

(b) Coagulation and dyselectrolytemia

- Massive blood loss and transfusion, along with excessive crystalloid administration (especially isotonic saline), can lead to dilutional coagulopathy and dyselectrolytemia.
- Any obvious bleeding should be looked for and treated.
- Dyselectrolytemia should be corrected.

(c) Hypothermia

- Causes: Bleeding, massive fluid and blood transfusion, anesthesia (dry gases, muscle relaxants, medication), surgical causes (evaporative cooling and lavage), and transport.
- Oxygen can be detrimental in patients with low cardiorespiratory reserve.
- Hypothermia may lead to tissue ischemia with delayed wound healing and increased surgical site infection. Other adverse effects include deranged coagulation and immunosuppression. Patients with coronary artery disease and those with vascular anastomoses and skin grafts are particularly vulnerable.
- Hypothermic patients with a core temperature less than 35 °C should be actively rewarmed with forced air rewarming devices, warm intravenous fluids, and adequate covering.

(d) Pain

- Appropriate and adequate pain relief is an essential component of postoperative care; these patients are no exception. Consultation with the pain management team is helpful.
- Pain should be assessed formally using a validated instrument such as VAS regularly. Analgesia should be titrated according to the patient's response.
- The modalities of pain relief usually available are:
  - Opioid analgesics such as morphine and fentanyl are used as iv aliquots as infusions or in patient-controlled analgesia (PCA) devices.
  - Intravenous paracetamol.
  - NSAIDs such as diclofenac (iv/im/rectal). These should be avoided in patients at risk of renal injury, including elderly patients and those who have intraoperative hypotension.
  - Intravenous tramadol.
  - Neuraxial local anesthetic/opioid combinations.
  - Intra-articular injection of local anesthetics/opioids.
  - Peripheral nerve blocks.

(e) Sedation and altered mental states
  - Causative factors include residual effects of anesthetic drugs, hypothermia, hyponatremia, and hypercarbia.
  - Rule out residual neural blockade using a neuromuscular junction monitor (train-of-four monitors).
  - Other abnormal behavior is usually due to the effects of medication and rarely due to hypoxia, acidosis, or hypotension. Depending on the clinical scenario, you may need to rule out hypoglycemia.
  - Reassurance and correction of underlying derangement are usually sufficient.

(f) Nausea and vomiting
  - Postoperative nausea and vomiting (PONV) after general anesthesia is very troublesome to the patient.
  - Management strategies include reducing the dose of opioids and alternative analgesics.
  - 4–8 mg ondansetron can be effective. Be aware of the occurrence of side effects such as arrhythmias and intractable headaches.

- Abdominal wounds are not always closed at the end of an operation. The clinician needs to determine if the skin or fascia has been left open and, if so, what kind of temporary closure is employed.

Step 4: Postoperative Fluid Resuscitation

Identify and Correct Fluid Imbalance

- Conventional intake–output charts do not reflect fluid balance in critically ill patients or postoperative patients.
- Stress due to surgery and pain causes an increased secretion of ADH and aldosterone resulting in a high incidence of SIADH. Fluid sequestration in the gut wall, and interstitial fluid accumulation due to increased capillary leak, cause fluid disturbances.
- A low urine output may not indicate hypovolemia. Alternative measures of volume status should be used such as using ICU beds with an in-built weighing facility, abdominal ultrasound assessment of IVC collapsibility, transthoracic echocardiography to assess filling of the left ventricle, or other dynamic measures of fluid responsiveness.
- Postoperative patients tend to retain free water. Hypotonic fluid administration should be restricted due to the risk of hyponatremia.
- In patients with chronic diuretic use, hypertension, and cardiac dysfunction, cautious use of diuretics could be tried if urine output remains low despite normal hemodynamics and no evidence of sepsis.
- Renal replacement therapy should be instituted as necessary, in consultation with the nephrology team.

Targets for Adequate Clinical Perfusion

- Mean arterial blood pressure > 70 mm Hg
- Heart rate < 100 beats/minute
- Warm, pink skin without cyanosis or mottling over the digits, thighs, or knees, with palpable pulses
- Good capillary refill
- Clear yellow urine >0.5–1 mL/kg/hour

Step 5: Identify and Correct Cardiac and Pulmonary Problems

- Pre- and intraoperative management
  - Cardiovascular status should be assessed and optimized preoperatively by careful preoperative cardiovascular and pulmonary risk assessment, optimizing medications, and other measures. These will include cessation of smoking, incentive spirometry, treatment of chest infections and bronchospasm, etc.
  - It is to be kept in mind that these measures are not possible in emergent surgeries.
  - The risk indices for postoperative complications such as that developed by Shoemaker for cardiac and others for pulmonary complications may be followed to identify patients at high risk (Table 22.1).
  - Validated surgical risk calculators may also be used.
  - These patients may be managed using perioperative goal-directed therapy using minimally invasive cardiac output monitoring techniques to improve outcomes.
- Postoperative management
  - High-risk patients should be monitored for chest discomfort/pain, ST segment changes, hemodynamic instability, and pulmonary edema. A low threshold

Table 22.1 Shoemaker criteria for identifying patients at high risk of cardiac complications

Patient factors
Prior severe cardiac illness, acute myocardial infarction (AMI), stroke, congestive heart failure (CHF)
Age more than 70 years
Severe sepsis with septic shock
Severe nutritional problems
Respiratory distress, chronic obstructive pulmonary disease, requiring mechanical ventilation
Acute hepatic failure and acute renal failure
Severe CNS problem—head injury with coma (Glasgow coma score < 8)
Surgical factors
Extensive ablative surgery for cancer, more than 8 h
Severe multiple trauma—three organs or two body cavities
Massive blood loss of more than 8 units
Acute abdominal catastrophe—peritonitis, perforated bowel with gangrene
Aortic aneurysm and end-stage vascular disease

for investigations such as 12-lead ECG and cardiospecific enzyme tests is useful.

  - Postoperative respiratory failure is usually due to one or more of the following:
    - Atelectasis
    - Aspiration
    - Pain leading to splinting of the diaphragm and hypoventilation
    - Tracheobronchitis and pneumonia
    - Noncardiogenic pulmonary edema
  - Measures to avoid pulmonary complications include:
    - Early ambulation and assisted coughing
    - Continuation of incentive spirometry
    - Intermittent positive pressure breathing exercises
    - Adequate hydration
    - Humidification of inspired air and oxygen
    - Noninvasive ventilation, especially in patients with COPD and hypercapnia
    - Measures to reduce risk of aspiration (positioning, minimizing the use of NG tube, prokinetics, etc.)
    - Optimizing analgesia and avoiding excessive sedation
    - Early identification and treatment of sepsis
    - Early external stabilization of long bone fractures using a damage-limitation philosophy

Step 6. Other Measures

- Transport patients safely with adequate monitoring, provide a structured handover, and use a documentation checklist.
- Early identification of ongoing hemorrhage by inspecting the volume and type of drain, monitoring for hemodynamic instability, and detecting falling hematocrit. Correct volume deficit, hypothermia, acidosis, coagulopathy, and thrombocytopenia.
- Identify the site of bleeding and prepare the patient for re-exploration if necessary, in consultation with the surgical team.
- Use blood and blood products judiciously. In a hemodynamically stable patient, without active bleeding or active coronary artery disease, keep the hemoglobin level at 7–8 g/dL.
- Identify sepsis early and use antibiotics judiciously. The institutional protocol should be followed as per established guidelines for perioperative antibiotic prophylaxis.
- Surgical patients are in a hypercoagulable state in the perioperative period. Institutional protocols should be followed for deep vein thrombosis prophylaxis. A combination of pharmacological and mechanical methods (pneumatic compression or graduated compression stockings) is advocated in patients at high risk.
- Early enteral nutrition should be instituted as soon as possible. If early enteral nutrition cannot be initiated, parenteral nutrition should be started especially in

Table 22.2 Risk factors for postoperative pulmonary complications

Age more than 50 years
Obesity
Smoking
Chronic obstructive pulmonary disease
Location of incision (upper abdominal, thoracic)
FEV_1 less than 1 L
FVC less than 1.5 L
FEV_1/FVC less than 30%
Use of pancuronium
Surgery lasting more than 3 h
Functional dependence
Serum albumin less than 3.5 g/dL

patients with established malnutrition. Consideration should be given to immunonutrition in patients with cancer surgery.

- Stress ulcer prophylaxis with H_2 blockers should be instituted in selected cases, i.e., patients on mechanical ventilation, those with a previous history of GI bleeding, or those on anticoagulants/aspirin.
- Thyroid status should be optimized in hypothyroid patients. Supplemental corticosteroids should be given to patients with a history of chronic use of systemic steroids.

There are certain risk factors that help predict postoperative pulmonary complications (Table 22.2).

Enhanced Recovery After Major Noncardiac Surgery (ERAS)

Goals include minimizing surgical stress responses, reducing end-organ dysfunction, providing optimal control of postoperative pain, expediting recovery, decreasing hospital length of stay, and reducing complications. It was originally proposed for colorectal cancer surgery but has since been extended to the postoperative setting of procedures such as duodenopancreatectomy, hepatectomy, esophagogastric surgery, radical cystoprostatectomy, etc.

The four key elements of this approach are comprehensive preoperative evaluation and preparation of the patient, optimum anesthesia and minimally invasive surgery to reduce the patient response to surgical stress, adequate postoperative management of the symptoms such as pain with early mobilization, and prompt reintroduction of a normal diet.

Suggested Reading

Guarracino F, Baldassarri R, Priebe HJ. Revised ESC/ESA guidelines on non-cardiac surgery: cardiovascular assessment and management. Implications for preoperative clinical evaluation. Minerva Anestesiol. 2015;81(2):226–33. Epub 2014 Nov 11. *This represents the official position of the ESC and ESA on various aspects of perioperative cardiac care, incorporating* *preoperative risk stratification based on preoperative assessment of functional capacity, type of surgery, cardiac risk factors, and cardiovascular function. They discourage indiscriminate routine preoperative cardiac testing*

Kakkos SK, Caprini JA, Geroulakos G, Nicolaides AN, Stansby G, Reddy DJ, Ntouvas I. Combined intermittent pneumatic leg compression and pharmacological prophylaxis for prevention of venous thromboembolism. Cochrane Datab Syst Rev. 2016;9:CD005258. https://doi.org/10.1002/14651858.CD005258.pub3. *Systematic review and meta-analysis of 22 trials and 9137 patients*

Puppo Moreno AM, Abella Alvarez A, Morales Conde S, Pérez Flecha M, García Urena˜ MÁ. La unidad de cuidados intensivos en el postoperatorio de cirugía mayor abdominal. Med Intensiva. 2019;43:569–77.

Sobol JB, Wunsch H. Triage of high-risk surgical patients for intensive care. Crit Care. 2011;15:217. https://doi.org/10.1186/cc9999. *This interesting article discusses preoperative evaluation and improved outcomes with ICU care and alternatives to ICU care*

van der Walt J, Joubert I. The pitfalls of postoperative theatre to intensive care unit handovers: a review of the current literature. South Afr J Anaesth Anal. 2014;20(3):143–6. https://doi.org/10.1080/22201173.2014.936776. *Highlights the importance of a structured postoperative handover protocol*

Specific Issues in Perioperative Care

23

Subhash Todi, Shrikanth Srinivasan, and Akhil Taneja

A 60-year-old male patient with triple-vessel disease with reduced left ventricular function and diabetes mellitus underwent coronary artery bypass graft (CABG) with extracorporeal support. He was transferred to the ICU, and his blood pressure was 90/60 mmHg on epinephrine infusion.

A 50-year-old male patient with a road traffic accident had undergone an emergency decompressive craniectomy due to an expanding intracerebral hematoma. He had arrived in the ICU postoperatively on the ventilator and was paralyzed. His blood pressure was 110/70 mmHg without any vasopressor support.

A 50-year-old male patient had undergone an emergent thoracotomy and left upper lobe resection due to massive hemoptysis not being controlled with conventional measures. He had arrived in the ICU ventilated with a saturation of 90% on FiO_2 of 0.8.

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Due to the increasing specialization of intensive care, patients with organ-specific surgery (thoracic, cardiac, neurosurgery) are being managed in dedicated ICUs. As these patients have specific perioperative problems, the intensive care physician taking care of these patients should have a working knowledge of their specific perioperative critical issues and should work in close consultation with the surgical and anesthetic team.

Cardiac Surgery

Traditionally, cardiac surgery has been performed via a median sternotomy incision with the use of a cardiopulmonary bypass (CPB) machine that maintains total body oxygenation and perfusion despite cardioplegia. After CPB is initiated, injection of a hyperkalemic cardioplegic solution directly into the coronary circulation produces a cardiac standstill. The cardioplegic solution also provides necessary nutrients for myocardial preservation despite the absence of cardiac blood flow. Traditional surgical approaches are associated with varying degrees of hypothermia, coagulopathy, and hemodilution. Usually, the patients need varying periods of mechanical ventilation postoperatively.

Minimally invasive surgery (MIS) modifies one or more of these techniques to accomplish similar surgical goals through small surgical incisions without CPB (i.e., off-pump), or both. MIS has been shown to reduce blood requirements, length of stay, and resource use. Patients often exhibit hemodynamic instability lasting approximately 12 to 24 hours, typically followed by a period of recovery.

Step 1: Take Handover Information from the Operating Room Staff

- Patient identification details
- Preoperative details
  - Type of coronary artery disease, valve dysfunction, left ventricular function, and pulmonary hypertension
  - Medications used—antiplatelets, anticoagulants, diuretics, angiotensin-converting enzyme inhibitors, statins, and calcium channel blockers
  - Comorbidities—diabetes, hypertension, peripheral vascular disease, stroke, renal dysfunction, and thyroid status
  - Preoperative functional capacity
  - Previous medical records
- Operation performed (on- or off-pump, arterial, venous graft) and problems encountered
- Current drug infusions
- Pacemakers and antiarrhythmic drug information

- Estimated blood loss, blood and blood product administered, and urine output
- Intraoperative fluid balance
- Antibiotics administered and timing
- Drains (number, placement)
- Latest arterial blood gas analysis, hematocrit, blood sugar, and electrolytes

Step 2: Checklist on Arrival of the Patient (A to I)

- *Airway*
  - The patient is connected to the ventilator.
  - Note the size of the tube, the position of fixation at the angle of mouth, and cuff pressure.
- *Breathing*
  - Look for chest movement. Auscultate and confirm air entry to both lungs.
  - The usual initial ventilator settings are as follows:
    - Breath rate of 12–15/min.
    - FiO2 of 0.6–0.8.
    - Tidal volume of 6–8 mL/kg.
    - Depending on the arterial blood gas (ABG) report, settings are modified subsequently.
- *Circulation*
  - Set up the monitor.
  - Check
    - ECG for rate, rhythm, and ST segment changes.
    - Arterial pressure, oxygen saturation.
    - Pulmonary artery pressure/central venous pressure—measure the pulmonary artery wedge pressure (PAWP), cardiac output (CO), and systemic vascular resistance.
    - Mixed venous oxygen saturation.
    - Temperature probe—if the temperature is less than 37 °C, a warming blanket should be placed.
    - Low urine output, acidosis, and peripheral examination are not a good indicator of the low perfusion state in these patients, and direct measurement of cardiac output is preferable in unstable patients.
- *Drugs*
  - Vasoactive drugs—check infusion pumps labeled with proper drug dosing and dilutions, and calculate infusion rate (mcg/kg/min).
- *Electrolytes*
  - Maintain K+ at 4–4.5 mmol/L.
  - Maintain Mg+ at 0.8–1.5 mmol/L.
- *Fluids*
  - Intravenous maintenance fluids (crystalloid) are started at the rate of 1–1.5 mL/kg/h.

  - Blood transfusion to keep hematocrit at more than 25–30%.
  - Maintain urine output at 0.5–1.0 mL/kg/h.
- *Glucose control*
- Maintain serum glucose between 140 mg and 185 mg/dl.
- Hypoglycemia should be avoided.
- Maintain Hemoglobin of 7.5–8 gm/dl.
- Prevent postoperative delirium.
- *Hemorrhage*
  - Causes of bleeding after cardiac surgery include:
    - Inadequate surgical hemostasis
    - Inadequate platelet number or function
    - Inadequate reversal of heparin
    - Dilutional coagulopathy
    - Hypothermia
  - Chest tubes are connected to underwater seals. If bleeding is significant, and the coagulation profile is normal, the patient needs to go back to the operation theater for re-exploration.
  - In adult patients, bleeding is significant when:
    - >400 ml for 1 h
    - >300 ml/hr. for 2 h
    - >200 ml/hr. for 3 consecutive hours
    - >100 ml/hr. for 4 consecutive hours
  - CPB may induce coagulation abnormalities in these patients and this may be the cause of excessive bleeding.
  - Anticoagulation protocols:
    - Valve surgery: Anticoagulation is maintained with intravenous heparin. With mechanical valve prosthesis, oral anticoagulants (warfarin) should be started as soon as oral intake is permitted (48–72 h). Initial overlapping therapy of warfarin with heparin is recommended for 48–72 h to prevent warfarin-induced hypercoagulability.
  - Coronary artery bypass graft—aspirin/clopidogrel in low doses is started as soon as oral feeds are started.
  - Reverse heparin effect by protamine if needed.
- *Investigations*
  - Investigations should be done within 30 min of arrival.
    - ECG
    - ABG
    - Hct and electrolytes
    - Chest X-rays—look for pneumothorax, hemothorax, position of endotracheal tubes, chest tubes, intravascular catheters, pacing wires, lung infiltrates, and cardiac size.
    - Coagulation profile (Prothrombin Time (PT), APTT, ACT)
    - Thromboelastogram (if available)

Step 3: Take General Care of the Patients

- Position—head end elevated at 30–45°
- Neurological assessment
  - Awake and obeying commands
  - Able to move all four limbs

Step 4: Look for and Manage Specific Complications

- The most common complications after cardiac surgery are mechanical complications, physiological complications (inadequate preload, excessive afterload, and poor ventricular pump function), mias, and myocardial infarction.
- *Arrhythmias* are common, occurring in 25–60% of patients. Advanced age, prior atrial fibrillation, and combined bypass graft/valve surgery are risk factors. Exclude precipitating causes such as hypoxia, hypercarbia, lack of analgesia, and electrolyte imbalance (hypokalemia and hypomagnesemia) before instituting antiarrhythmics. Treat arrhythmias only if hemodynamically significant. Arrhythmias with signs of ischemia may signal perioperative infarction, inadequate revascularization, and blocked graft requiring urgent reoperation.
- *Low-output state*: Keep a high index of suspicion if unexplained postoperative hypotension, tachycardia, or pulmonary edema occurs. An urgent echocardiogram should be performed to exclude pericardial tamponade. Assess left ventricular function and volume status.
  - In cases of pericardial tamponade, the patient should be re-explored with the evacuation of hematoma. The chest may have to be reopened in the ICU if tamponade is sudden and severe, leading to hemodynamic collapse.
  - In low-output states, rewarming should be gradual. Decrease metabolic demand by proper analgesia, sedation, and muscle relaxants to decrease shivering. Optimize preload by judicious use of fluid and blood (keep hematocrit 0.25–0.35) under monitoring. Add inotropes and if blood pressure permits decrease afterload by adding vasodilators. Due to ischemia-reperfusion injury, a phase of stunned myocardium persists, which usually resolves over a variable period and is helped by inotropic support. This phenomenon should be distinguished from ongoing ischemia where inotropic support is detrimental.
  - An intra-aortic balloon pump is sometimes used to maintain coronary perfusion in low-output states.
- *Postoperative hypertension*: It is usually transient but may lead to left ventricular dysfunction, myocardial ischemia, graft and suture line disruption, and increased bleeding. Ensure proper analgesia and sedation. Parenteral vasodilators like nitrates may be used.
- *Atelectasis:* Ensure early mobilization and incentive spirometry.
- *Fluid overload*: Maintain a strict input–output chart. Low-dose diuretics may be needed.

- *Myocardial ischemia* or *infarction* may be difficult to diagnose in postoperative settings as ECG, echocardiogram, and cardiac enzyme may not be able to detect early ischemia and may be false positive.
- *Right ventricular dysfunction*: This may occur due to pulmonary hypertension or ischemic reperfusion injury. It presents with low cardiac output syndrome, which may initially be volume responsive. The patient has high right-sided filling pressure disproportionate to left-sided pressure, low cardiac index, and low systemic blood pressure. It is managed by maintaining sinus rhythm, appropriate heart rate (by pacing if necessary), optimizing preload, reducing afterload (with pulmonary vasodilators such as inhaled nitric oxide or epoprostenol infusion), inotropic support, and mechanical assist devices if needed.
- *Significant neurological deficit:* It occurs in 2–3% of patients undergoing coronary artery bypass surgery. This can present as stroke, transient ischemic attack, or global cerebral dysfunction. Early recognition is important.
- Prevent the occurrence of renal failure: Acute kidney injury occurs in up to 30% of patients and is associated with increased mortality. The best strategy is to prevent AKI. Optimize renal perfusion (avoid hypotension and hypovolemia), and avoid nephrotoxic drugs.
- Pulmonary dysfunction: Pleural effusion, atelectasis, pneumonia, difficulty weaning, diaphragmatic dysfunction and ARDS.

Step 5: Take a Fast-Track Approach to Extubation

- The increasing use of off-pump surgery, short anesthesia, and lower doses of sedatives has led to the early liberation of patients from ventilators. Many patients can be extubated within 4 h of surgery or even in the operating room.
- Plan for extubation within six hours of arrival in the ICU for most patients, by using short-acting sedatives such as dexmedetomidine or propofol.
- Use opioids judiciously to manage pain. For patients who are not candidates for early extubation, continuous fentanyl infusion for analgesia should be started.
- The key to a successful fast-track program is proper patient selection, high-level supervision by a disciplined team, and the absence of surgical complications.

Thoracic Surgery

Step 1: Take Care of Immediate Postoperative Issues

- Immediate concerns include assessment of oxygenation, volume status, cardiovascular support, provision of ventilatory support if needed to ensure adequate oxygen delivery and status of chest drains that accompany the patient from the operating room.
- Special concerns apply to pain control, which is especially important, as pain will limit respiratory effort and can also precipitate delirium and agitation.

Step 2: Be Cognizant of Potential Problems Following Thoracotomy

- Poor respiratory effort and sputum retention (chest wall trauma and pain)
- Atelectasis, pneumonia, and sepsis
- Alveolar and minor bronchial air leaks
- Localized or generalized pulmonary edema
- Intercostal, pulmonary, or bronchial vessel hemorrhage
- Cardiac arrhythmias, myocardial infarction, and heart failure
- Pulmonary and systemic embolism
- Chest wall hematoma, wound infection, and wound dehiscence

Step 3: Be Cognizant of Potential Problems Following Lung Resection

- Respiratory insufficiency due to extensive lung resection
- Bronchopleural fistula and massive air leak
- Early and late mediastinal shift
- Atrial fibrillation and other supraventricular arrhythmias
- Torsion of lobe or segment
- Cardiac herniation (usually after pneumonectomy with a partial pericardium excision, when the heart herniates through a gap in the pericardium; may be manifested by supraventricular arrhythmias and/or severe hypotension)
- Residual venous or arterial lung infarction
- Blood loss into the pleural space, mediastinum, or bronchus
- Bronchial obstruction from accumulated secretions, blood, and pus
- Empyema following air leaks, insufficient lung volume, or overwhelming sepsis
- Paradoxical chest wall movement following extensive rib resection
- Pulmonary hypertension and acute right-sided heart failure

Step 4: Get a Chest X-ray of the Hypoxic Patient

- In all postoperative thoracic surgery patients who are hypoxic on arrival, after a careful physical examination, urgent chest X-rays should be requested.
- A daily chest radiograph must be performed in unstable patients, to confirm endotracheal, nasogastric, and chest tube placement, as well as to identify any pneumothorax, mediastinal shift, or significant atelectasis.

Step 5: Assess Chest Drain Sites and the Amount of Drainage

- Hourly output from chest tubes should be recorded, and the operative team should be notified if drainage is greater than 100 mL/h for more than 4 h, or if greater than 200 mL of drainage is recorded in any 1-h observation period.

- Expected chest tube drainage from major thoracic procedures in the first 24 h is roughly 300–600 mL, tapering to less than 200 mL by the second day.
- Daily chest radiographs are usually obtained while chest tubes are in place.
- Once all air leaks resolve and drainage is minimal (<100 mL/24 h), chest tubes may be removed during the expiratory phase of ventilation or while the patient performs a Valsalva maneuver.
- After pneumonectomy, surgeons usually keep the intercostals drain on the operated side clamped so that the fluid fills the pneumonectomy space and maintains the mediastinum central.
- This drain may be occasionally unclamped for a short period to note whether there is bleeding.
- The drain may need to be unclamped if there is a very rapid accumulation of fluid in the pneumonectomy space, manifested by dyspnea, mediastinal shift to the opposite side, high jugular venous pressure (JVP), or central venous pressure. This may be mistaken for congestive cardiac failure.

Step 6: Address Airway Concerns and Plan for Extubation

- Extubation can often be accomplished in the operating room, but continued ventilation may be necessary in the presence of concurrent cardiac illness, inability to protect the airway, malnutrition, or coexisting lung disease.
- Ideally, the patient should be awake and following instructions and have an adequate gag reflex (signifying airway protection) and cough (for secretion clearance).

Step 7: Control Pain

- Adequate pain control is important not only to ensure patient comfort but also to avoid potential cardiac and pulmonary complications. Early pain management is also important in an effort to reduce the chances of developing long-term post-thoracotomy pain.
- Various options exist for pain management. They include systemic analgesics, neuraxial opioids, and local anesthetics via the epidural route, regional anesthesia such as intercostal and paravertebral nerve blocks, and adjuvant therapies such as transcutaneous electrical nerve stimulation (TENS) or applied heat. Exercise caution when using TENS in a patient with a temporary pacemaker in situ as it may interfere with the sensing function of the pacemaker.
- The mainstay of postoperative pain control is systemic analgesics in the form of opioids. Agents such as morphine and fentanyl are frequently used, with the intravenous route providing the most predictable responses. Opioid side effects remain the greatest issue, with respiratory depression, nausea, vomiting, and ileus being the most common.

- Nonopiate medications such as paracetamol and nonsteroidal anti-inflammatory drugs (NSAIDs) are reasonable adjuncts to opioids. Because NSAIDs may exacerbate renal dysfunction, it is necessary to exercise caution when using them in the presence of underlying renal insufficiency.
- Neuraxial opioids and local anesthetics via the epidural route provide excellent regional pain control. Epidural catheters are the preferred route, and when local anesthetics, either with or without opioids, are infused in this manner, the incidence of pulmonary complications decreases relative to that with systemic opioids.
- In addition, patients requiring prolonged postoperative mechanical ventilation may benefit from the centrally acting α-adrenergic agonist, dexmedetomidine, as an analgosedative.

Step 8: Optimize Fluid Balance

- Fluid management in the postoperative period requires special attention due to the high risk for pulmonary edema.
- Traditional markers of perfusion help determine if a patient is adequately volume-resuscitated. These include urine output (usually >0.5 mL/kg/h), mental status, blood pressure, heart rate, blood lactate level, capillary refill time, venous oxygen saturation, filling pressures, and cardiac performance.
- Ideally, the clinician should limit crystalloid infusion to 20 mL/kg for the first 24 h.

Step 9: Start Respiratory Therapy

- Thoracic surgical patients often have significant underlying chronic obstructive pulmonary disease, impaired mucociliary clearance, excessive secretions, and/or increased closing volumes, all of which predispose to atelectasis.
- The respiratory therapist plays an important role in providing secretion management and performing chest physiotherapy (percussion and vibration) and incentive spirometry.
- Other modalities supporting recovery include adequate hydration, aerosolized bronchodilators, humidified oxygen, and early identification and treatment of infection of the tracheobronchial tree.
- Chest physiotherapy should begin as soon as the patient has recovered sufficiently from anesthesia to cooperate.

Step 10: Manage Bronchopleural Fistula

- Early postoperative bronchopleural fistula in a pneumonectomy patient is a surgical emergency. The typical presentation is sudden expectoration of copious amounts of pink, frothy sputum, which may be misdiagnosed as pulmonary

edema. Further management will likely include bronchoscopy to assess the stump closure and immediate reoperation if a leak is detected.
- A double-lumen tube may need to be introduced to prevent soiling of the opposite lung by contents of the pleural space and to prevent loss of tidal ventilation through the fistula.
- Always insert an intercostal drain on the side of the fistula and keep it draining at all times.

Step 11: Manage Postoperative Hypoxemia

- Postoperative hypoxemia is common and may be due to hypoventilation, atelectasis, aspiration, sepsis, acute respiratory distress syndrome, pneumonia, or pulmonary embolization.
- Noninvasive ventilation or High Flow Nasal Oxygen may be useful to treat respiratory failure after lung surgery.
- If pulmonary emboli are suspected, manage the patient accordingly.
- Systemic tumor emboli, though uncommon, may be seen after pulmonary resections for primary bronchogenic carcinomas or metastatic sarcomas.
- Meticulous attention must be given to prevent dehydration, overtransfusion, and infection.

Step 12: Address Special Concerns in Esophageal Surgery

- Patients who undergo esophageal resection for carcinoma tend to be malnourished and have complications, including atelectasis, pneumonia, aspiration, and retained secretions.
- One-third of patients experience respiratory complications. The most dreaded complication of esophageal surgery is leakage from the surgical site. Factors impacting the incidence include high estimated intraoperative blood loss, cervical location of the anastomosis, and the development of postoperative acute respiratory distress syndrome.
- Anastomotic dehiscence or ischemia of the gastric tube should be suspected when the following signs/symptoms appear: hydropneumothorax, bronchospasm, atrial fibrillation, dyspnea, hypotension, raised lactate levels, and tachycardia.
- Mortality associated with anastomotic leaks is historically high, but with improved surgical techniques, the patients now have a more promising outcome.
- Intraoperative nasojejunal tube placement or jejunostomy is vital to maintain enteral nutrition throughout the postoperative period.
- A multimodal approach including epidural analgesia, judicious fluid administration, early mobilization, and enteral nutrition contributes to a good outcome.

Neurosurgery

Step 1: Maintain Airway, Oxygenation, and Ventilation

- Adequate oxygenation is mandatory for proper neuronal functioning. Hypercarbia is detrimental to the brain injury patient as it leads to a rise in intracranial pressure (ICP), and therefore proper ventilation should be ensured (see Chap. 31, Vol. 1).
- Maintain arterial oxygen saturation of more than 94% and PaCO2 in the normocapnic range. Reserve hyperventilation for management of sudden increases in the ICP.

Step 2: Maintain Adequate Fluid Balance While Preventing Brain Swelling

- Avoid hypotonic fluids (like 5% dextrose) to prevent brain swelling. Note that lactated Ringers' solution is also mildly hypotonic.
- Use isotonic fluid like normal saline to maintain euvolemia.
- Fluid restriction and active diuresis should be avoided as they will lead to reduced circulating blood volume and hypoperfusion of the brain.
- Maintain normal or slightly high serum sodium values (145–150 mEq/L).

Step 3: Maintain Normoglycemia

- Hyperglycemia is associated with worse outcomes after brain injury. This is because during low oxygen supply state intracellular sugar is converted into lactate, which causes intracellular acidosis and is detrimental to neuronal cells.
- On the other hand, for normal neuronal function, a continuous supply of glucose is mandatory and hypoglycemia is equally detrimental.
- Thus, a fine balance of glucose control between 140 and 180 mg/dL should be maintained, with insulin infusion and ensuring adequate carbohydrate intake.

Step 4: Treat Fever Aggressively

- Fever is detrimental to brain tissues, and on the other hand, mild hypothermia is beneficial.
- Any febrile episode should be actively controlled with antipyretics and external cooling measures.

Step 5: Maintain Blood Pressure in the Normal Range

- Excessive swings of blood pressure should be avoided as autoregulation of cerebral blood flow is disrupted with the injured brain and flow will increase or decrease with changes in blood pressure leading to hyperemia with increased ICP during hypertension or hypoperfusion leading to decreased cerebral blood flow and neuronal injury during hypotension. Mean arterial pressure should be kept in the range of 65–75 mmHg in most patients.

Step 6: Decrease Cerebral Metabolic Demand

- Judicious use of sedatives (e.g., barbiturates and propofol) and analgesics is useful in these cases.

Step 7: Prevent and Treat Convulsions Aggressively (See Chap. 30, Vol. 1)

- Anticonvulsant prophylactic may be given perioperatively for cortical surgeries.
- All episodes of new-onset seizures should be actively managed to prevent secondary brain injury.
- In patients with persistent or fluctuating levels of consciousness, nonconvulsive status should be ruled out.
- Patients with pre-existing seizure disorder need to have antiseizure medication continued perioperatively, with as little disruption as possible.

Step 8: Monitor the Patient for Increases in ICP and Neurological Deterioration Frequently (See Chap. 37, Vol. 1)

- Hourly Glasgow coma score, pupillary size, and reaction.
- ICP monitoring where appropriate.
- Maintain CPP (MAP−ICP > 65 mmHg).
- Measurement and management of raised ICP (refer to Chap. 37, Vol. 1).
  - Basics
    Normal ICP is less than 15 mmHg.
    Raised ICP is more than 15–20 mmHg for more than 1–5 min.
    CPP = MAP − ICP.
    Always measure cerebral perfusion pressure (CPP) along with ICP.
    The ICP monitor (intraventricular drain or subarachnoid bolt) is inserted if indicated.
    The transducer (without a flush system) has to be kept at a midventricular level, which is at the level of tragus in the supine position.

    Start treatment if ICP is more than 20–25 mmHg for more than 5 min.
  - Management of intraventricular drain (IVD)
    Drain cerebrospinal fluid (CSF) whenever ICP is more than 15–20 mmHg.
    Drain CSF until ICP is 10–15 mmHg.
    Measure daily CSF drain required to maintain ICP.
    Examine CSF every day.
    Take full sterile precautions.
    Lumbar drain
  - If IVD is in situ, do a lumbar puncture and compare opening and closing ventricular and lumbar pressures.
  - If there is a comparable drop, IVD can be removed, and CSF is drained by lumbar punctures (LPs).
  - If there is no fall in ventricular pressures, drain CSF from IVD and avoid further LPs.
- Approach to an acute rise of ICP in a previously stable patient
  - Check the transducer level and re-zero.
  - Confirm the waveform of the ICP trace.
  - Position the head, neck, and endotracheal tube tape properly to minimize an increase in ICP.
  - Check ventilation, ABG, and X-rays and increase mechanical ventilation to decrease pCO2 if necessary.
  - Exclude anxiety, pain, or seizures.
  - Drain CSF or give mannitol bolus.
  - Perform a CT scan if appropriate.

Suggested Reading

Allou N, Bronchard R. Risk factors for postoperative pneumonia after cardiac surgery and development of a preoperative risk score*. Crit Care Med. 2014;42(5):1150. *Multivariate analysis identified four risk factors for postoperative pneumonia: age (odds ratio), chronic obstructive pulmonary disease, preoperative left ventricular ejection fraction, and the interaction between RBC transfusion during surgery and duration of cardiopulmonary bypass. A 6-point score including the three preoperative variables then defined two risk groups corresponding to postoperative pneumonia rates of 1.8% (score* < 3*) and 6.5% (score* ≥ 3*)*

Behera BK, Puri GD. Patient-controlled epidural analgesia with fentanyl and bupivacaine provides better analgesia than intravenous morphine patient-controlled analgesia for early thoracotomy pain. J Postgrad Med. 2008;54(2):86–90. *Significantly less number of patients required rescue analgesia in the PCEA group (*$P < 0.05$*). Pain relief was better both at rest and during coughing (*$P < 0.05$*) in the PCEA group as compared to IVPCA. Patients in the PCEA group were less sedated and had fewer incidences of side effects, that is, nausea/vomiting and pruritus*

Bláha J, Mráz M, Kopecký P. Perioperative tight glucose control reduces postoperative adverse events in nondiabetic cardiac surgery patients. J Clin Endocrinol Metab. 2015;100(8):3081–9. *Perioperative initiation of intensive insulin therapy during cardiac surgery reduces postoperative morbidity in nondiabetic patients while having a minimal effect in diabetic subjects*

Karamichalis JM. Cardiovascular complications after lung surgery. Thorac Surg Clin. 2006;16(3):253–60. *Although postoperative cardiac events cannot be completely eliminated* *from the thoracic surgery population, the prevention, treatment, and follow-up strategies outlined can attenuate these significant morbid and mortal events*

Landoni G, Lomivorotov VV. Levosimendan for hemodynamic support after cardiac surgery. CHEETAH Study Group. N Engl J Med. 2017;376(21):2021–31. *In patients who required perioperative hemodynamic support after cardiac surgery, low-dose levosimendan in addition to standard care did not result in lower 30-day mortality than placebo*

Soto RG, Fu ES. Acute pain management for patients undergoing thoracotomy. Ann Thorac Surg. 2003;75(4):1349–57. *This work provides a review of the literature and recommendations for the clinician*

Venkataraman R. Vascular surgery critical care: perioperative cardiac optimization to improve survival. Crit Care Med. 2006;34(9 Suppl):S200–7. *Perioperative addition of statins to β-blockers in high-risk patients undergoing vascular surgery merits further evaluation. Preoperative coronary revascularization should be restricted to patients with unstable cardiac symptoms*

Part VII

General Issues

Initial Assessment and Resuscitation

24

Jeetendra Sharma and Apoorva Tiwari

A 52-year-old male patient with a history of chronic active alcoholism and history of endoscopic variceal ligation (EVL) for Grade III esophageal varices 2 years back was admitted to ICU with complaints of upper gastrointestinal bleeding and altered sensorium. His vitals on arrival were axillary temperature of 37.0 degrees, non-invasive BP of 80/51 mm Hg, rapid thready pulse with a rate of 142/min, and respiratory rate of 27/min with SPO2 of 87% on ambient air with Glasgow Coma Scale (GCS) of 12.

Managing a patient in the ICU arriving in a morbid condition is a challenging task. The underlying concept is that timely intervention is directly proportional to reducing morbidity and mortality. A prompt and protocolized resuscitation regimen will help salvage these patients.

Step 1: Assign Responsibilities

- Quickly make a team and assign job responsibilities to every member clearly and appropriately. Effective close-loop communication should be established.
- In the initial phase, the patient should be seen by a senior member of the ICU team for initial resuscitation, investigation, management planning, and family briefing.
- Assign two doctors for initial resuscitation.
- Assign two nurses initially for unstable patients.
- Take early assistance whenever needed from other members of the team.

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Step 2: Start Initial Assessment and Resuscitation

- The initial aim is to identify and address life-threatening conditions. Correction of physiological abnormalities should take precedence over arriving at an accurate diagnosis.
- Follow ACLS protocols immediately following cardiac arrest or near cardiac arrest.
- Pertinent history taking, physical examination, sending investigations, and resuscitation need to be carried out simultaneously rather than sequentially as time is limited.
- Resuscitation should be systematic for hemodynamically unstable patients and aimed at assessing and managing A (airway), B (breathing), and C (circulation).
- All three components can be managed simultaneously; a sequential approach is not necessary.

Airway (A)

- Assess the airway. The need for definitive airway by endotracheal intubation or airway adjunct (oral/nasal airway), supralaryngeal devices, or surgical cricothyrotomy in a patient is mainly based on clinical assessment and should not be delayed.
- Ask for assistance whenever in doubt about a difficult airway.
- Look, listen, and feel for signs of airway obstruction and secure the airway and intubate when necessary (for details, see Chap. 1, Vol. 1).
  - Snoring—due to upper airway obstruction by tongue and oropharyngeal soft tissue—insert oro/nasopharyngeal airway.
  - Gurgling—due to upper airway obstruction by secretions—perform suctioning.
  - Stridor—due to obstruction by a foreign body or stenosis of the upper airway, usually inspiratory—remove the foreign body or intubate.
  - Wheeze—due to spasms in small airways—give bronchodilators.
  - Complete airway obstruction is silent—intubate.

Breathing (B)

- Assess the need for oxygen and ventilation. It can be assessed clinically along with pulse oximetry and arterial blood gas analysis:
- Look for clinical signs of respiratory distress:
  - Breathlessness, dyspnea
  - Tachypnea
  - Inability to talk
  - Open-mouth breathing

Table 24.1 Clinical features of inadequate oxygenation

Restlessness Delirium Drowsiness Cool extremities Cyanosis	Tachycardia Arrhythmia Hypotension Flapping tremor (asterixis)

  - Flaring of ala nasi
  - Use of accessory muscles for respiration
  - Suprasternal indrawing
  - Paradoxical breathing (inward movement of the abdomen during inspiration)
- Look for clinical features suggestive of inadequate oxygenation or ventilation (Table 24.1).
- Remember that these clinical presentations are late manifestations of respiratory failure and imply impending cardiorespiratory arrest. Patients need to be identified much earlier, and appropriate management should be instituted.
- Look for features of tension pneumothorax and evidence of massive pleural effusion or hemothorax and drain immediately.
- Any evidence of massive lung collapse with desaturation requires intubation, suctioning, and positive-pressure ventilation.
- Some clinical conditions, for example, deep unconsciousness (GCS <8), severe hemodynamic instability, or severe respiratory distress, require immediate endotracheal intubation and mechanical ventilation.
- Noninvasive ventilation can be tried in relatively stable patients if they are suffering from a condition where noninvasive ventilation is effective.
- Use High Flow oxygen device whenever indicated.
- Normal oxygen saturation does not exclude compromised airway and the need for intubation and ventilation.

Circulation (C)

- Assess the adequacy of circulation. Assessment and management should go side by side.
- Examine the following:
  - Peripheral and central pulse for rate, regularity, volume, and symmetry
  - Skin temperature (cold clammy skin is a sign of shock)
  - Heart rate and rhythm
  - Blood pressure (supine and sitting for orthostatic hypotension)
  - Capillary refill
  - Jugular venous pressure
  - Mental status
  - Urine output

- Early volume challenge by intravenous fluid boluses or passive leg raising is appropriate in most hypotensive patients.
- Bedside echocardiography—e-FAST (Extended Focused Assessment with Sonography in Trauma), POCUS (Point-of-Care Ultrasound), or FATE (Focus Assessed Transthoracic Echocardiography)—can be performed.
- Consider invasive monitoring—invasive arterial pressure, central venous pressure monitoring, intrabdominal pressure monitoring, cerebral pressure monitoring, and advanced hemodynamic monitoring. Advanced hemodynamic monitoring not only guides fluid, inotropes, and vasopressor administration but also helps in making a diagnosis.
- Identify shock and classify it into different categories like cardiogenic, obstructive, distributive, and hypovolemic. Combined categories of shock are frequently encountered in acutely unstable patients.
- Hemodynamic instability or cardiac arrest attributable to acute pulmonary embolism needs urgent intravenous thrombolysis.
- Patients presenting with symptoms and signs suggestive of aortic dissection should have urgent control of blood pressure and heart rate and should be urgently investigated to confirm diagnosis.
- Apply sepsis bundle without delay in patients presenting with clinical features of sepsis or septic shock. Prompt appropriate antimicrobial administration intravenously is a part of the initial management of sepsis.
- Manage anaphylactic shock with intramuscular epinephrine.
- Neurogenic shock due to spinal cord injury may mimic distributive shock.

Disability—Neurological (D)

- Frequent neurological examination needs to be performed in drowsy patients.
- Hypoglycemia identification and its rapid correction are the rule of thumb in all acutely drowsy or unconscious patients. Empiric intravenous dextrose can be administered if blood sugar measurement is not possible within a few minutes.
- Lateralizing features like hemiplegia are usually a feature of neurological disease.
- A depressed consciousness level in the absence of a primary neurological cause is indicative of severe systemic disease.
- Control ongoing seizures with appropriate measures.
- Consider urgent antibiotics for patients with features suggestive of bacterial meningitis.
- High spinal cord injury may present as neurogenic shock

Exposure and General Examination (E)

- Expose the patient in privacy under controlled temperature and perform a speedy examination directed toward the identification of 7Hs and 5 Ts (Table 24.2).

Table 24.2 Reversible causes of unstable patient may lead to cardiac arrest

7H	5 T
Hypovolemia Hypoxia Hydrogen ion excess (acidosis) Hypoglycemia Hypokalemia Hyperkalemia Hypothermia	Tension pneumothorax Tamponade—cardiac Toxins Thrombosis (pulmonary embolus) Thrombosis (myocardial infarction)

Step 3: Take a Focused History

- A working diagnosis is essential to formulate a definitive treatment plan therefore attempts must be made to diagnose the disease process simultaneously, and on priority after the restoration of physiological parameters.
- Obtain history from relatives, doctors, nurses, and other medical staff in the unstable patient.
- Review patients' clinical charts and perioperative notes.
- Presenting problems in chronological order with duration and temporal profile of illness needs to be documented.
- Enquire about mechanism of injury in trauma patients.
- Ask for significant comorbidities such as cardiac, pulmonary, renal diseases, previous surgery, or any other significant past medical problem.
- Enquire about previous hospitalization or use of NIV at home.
- Enquire about baseline functional state (bedbound, ambulatory with support or independent), previous hospitalization, oxygen supplement, or use of noninvasive ventilation at home.
- In the elderly, enquire about usual mental state and cognition and assess frailty.
- Take detailed medication history with doses and duration. Do not forget to note any recent change of medication, drug allergies, over-the-counter medications, alternative medication, and self-administration of medications.
- Ask for any routine use of sedatives or psychiatric medication and other addictions, for example, alcohol, tobacco, etc.
- An "issue list" of active and inactive problems needs to be documented in the clinical notes.
- Ascertain patients' resuscitation status as per the family's wish or advanced directive from the patient.

Step 4: Perform a Focused Physical Examination

- Check for vital signs.
- Look for warning signs of severe illness (Table 24.3).
- Examine for any life-threatening or limb-threatening abnormalities systematically.

Table 24.3 Warning signs of severe illness

BP systolic <90 or mean arterial pressure < 60 mmHg
Glasgow coma score < 12
Pulse rate > 150 or < 50 beats/min
Respiratory rate > 30 or < 8/min
Urine output <0.5 mL/Kg/h

- Examine for pallor, cyanosis, jaundice, clubbing, or pedal edema.
- Examine skin for rash, petechiae, urticaria, and eschar.
- Examine other organ systems systematically.
- Examination needs to be repeated frequently for any new features or findings missed previously. In neurological patients, the Glasgow coma score needs to be assessed frequently. Similarly in trauma patients, repetition of the secondary survey is mandatory to discern missed injuries.
- Patients should be fully exposed in proper privacy during the initial examination.
- A detailed physical examination should be performed later once the patient stabilizes after initial resuscitation.

Step 5: Order Investigations

- Complete blood count, blood sugar, sodium, potassium, urea, creatinine, aspartate transaminase (AST), alanine transaminase (ALT), PT, APTT, arterial blood gas, and lactate level in septic patients are important initial investigations.
- Chest X-rays and a 12-lead ECG should be performed.
- Appropriate microbiology cultures should be sent.
- Further investigations should be based on findings from history and physical examination.
- In unstable patients, investigations should be performed at the bedside as much as possible.
- If transport outside the ICU is needed, the patient should be properly monitored and accompanied by qualified personnel (see Chap. 31, Vol. 2).
- Maintain an investigation flow sheet in chronological order.
- Critical values (high/low) in investigations require immediate corrective actions (Table 24.4).

Table 24.4 Examples of investigations requiring urgent corrective action

Blood sugar <80 mg/dL or > 600 mg/dl
Sodium <110 or > 160 mmol/L
Potassium <2.5 or > 6.0 mmol/L
pH < 7.2
Bicarbonate <16 mmol/L

Step 6: Recognize the Patient at Risk

- Take special precautions in the following group of patients:
  - The elderly and immunocompromised may not show features of decompensation such as fever and tachycardia.
  - Polytrauma patients, due to multiple injuries and the effect of distracting pain, are difficult to assess.
  - In young adults, decompensation is late due to physiological reserve.

Step 7: Assess Response to Initial Resuscitation

- Assess changes in vital signs with initial resuscitation—pulse rate, rhythm, blood pressure, oxygen saturation, urine output, and mental state.
- Continuous assessment is mandatory, and one needs to be vigilant and present at the bedside.
  - Preload assessment and volume responsiveness with bedside 2 D Echo, SVV, PPV, PLR, etc.
  - Repeat arterial blood gas at a timely interval.
  - Comprehensive hemodynamics and neurological monitoring.

Step 8: Assess the Intensity of Support

- Inspired oxygen fraction needed to maintain saturation above 90%.
- Intensity of ventilatory support—positive end-expiratory pressure, minute ventilation.
- Dose of vasopressor and inotrope needed to maintain mean arterial pressure above 60 mmHg.
- Need for volume support to keep adequate urine output.
- Need for blood transfusion to keep hemoglobin above 7 gm/dL.
- Need for sedation in agitated patients.
- Need for dialysis support.
- Need of temporary intravenous pacemaker.
- Refractory cardiogenic shock may require urgent veno-arterial extracorporeal membrane oxygenation (VA ECMO).
- Refractory severe hypoxia in ARDS may necessitate venovenous extracorporeal membrane oxygenation (VV ECMO).

Step 9: Seek Help for Specific Problems that Require Expertise (Specialty Consultations)

- Cardiologist—complete heart block, acute coronary syndrome, cardiogenic shock, intra-aortic balloon pump insertion, pericardial tamponade, massive pulmonary embolism
- Nephrologist—need of urgent renal replacement therapy
- Neurologist—acute stroke or undiagnosed depressed conscious level
- Neurosurgeon—intracranial hemorrhage, head injury, severe cerebral edema
- Gastroenterologist—for gastrointestinal bleed
- Trauma surgeon—polytrauma, abdominal trauma, thoracic trauma, compartment syndrome
- Obstetrician—ruptured ectopic pregnancy, postpartum hemorrhage
- Intervention radiologist—control of ongoing hemorrhage by vascular embolization
- Cardiothoracic surgeon/ECMO team—ECMO installation

Step 10: Construct a Working Diagnosis and Plan for Further Management

- Initial resuscitation, assessment, investigation, and response are helpful in arriving at a working diagnosis or making ground for a differential diagnosis.
- Reassess the patient frequently to modify the initial plan if needed.
- Problem-oriented goals to be defined and steps to achieve these goals within stipulated time must be incorporated in the plan of management (Tables 24.5 and 24.6).

Table 24.5 Examples of the plan of management with a list of relevant goals[a]

Goals	Plan
Mean arterial pressure > 65 mm Hg	Continuous invasive arterial blood pressure monitoring Appropriate fluid resuscitation Vasopressor/inotropic support if required
Hb >7 mg/dl	Monitoring of Hb level in blood 8 hourly Packed red cell transfusion if Hb < 7gm/dl
Blood platelets count >10,000 per cu. mm	Monitor blood platelet count 8 hourly Watch for bleeding; if it occurs, transfuse one unit of single donor platelets collected by apheresis (SDP) If platelets count <10,000 cu. Mm, transfuse one unit of SDP 4–6 units of random donor platelets collected from multiple donors (RDP) may be transfused if SDP is not immediately available
PaO2 > 65 mm Hg	Use oxygen supplementation methods—prongs/mask Consider NIV/invasive ventilatory support/high flow nasal cannula (HFNC)

(continued)

Table 24.5 (continued)

Goals	Plan
Adequate and smooth breathing	Provide ventilatory support with endotracheal intubation if GCS < 9 Bronchodilator nebulization if bronchospasm Breathing exercises Chest physiotherapy Noninvasive ventilation where indicated
Conscious and alert	Close neurological monitoring Consider CNS imaging Consider osmotic therapy
Urine output >30 ml/hour	Ensure adequate resuscitation Consider renal replacement therapy
Sedation score = 0–1	Adjust infusion rate of sedative according to sedation score Every day sedation interruption
Intra-abdominal pressure (IAP) < 12 mm hg	Continuous IAP monitoring Apply nonsurgical measures to reduce IAP Consider surgical intervention if medical measures fail to reduce IAP

[a]Please note this list is not comprehensive

Table 24.6 Framework for the plan of management of critically ill patients

Categories of plan	Common examples
Plan related to monitoring and investigations	Invasive BP, CVP, IAP, ICP, ABG, biochemistry investigation, microbiology investigations, radiology investigations, echocardiography study, endoscopic study
Plan related to treatment initiation/modification	Vasopressors, inotropes, antibiotics, antihypertensive, antiepileptics, blood products
Plan related to general measures	Oxygen supplement, respiratory support, ventilatory setting, positioning of patient, nutrition, diet specification, noise restriction, pain management, oral hygiene, pressure injury prevention, infection control general and specific measures
Plan related to procedure/intervention/surgery	Intubation, CVL placement, arterial line placement, ICD placement, pacemaker placement, coronary intervention, laparotomy, neurosurgery, wound debridement, radiological interventions
Plan related to specialty consultations	Cardiology, neurology, gastroenterology, endocrinology, nephrology, general surgeon, CTVS surgeon, gynecology, obstetrics, urology

Step 11: Brief Relatives

- After initial resuscitation, assessment, investigation, and response, the family should be briefed about the likely diagnosis, treatment plan, approximate prognostication, and duration of stay, and consent should be taken for any invasive procedures.

Step 12: Documentation and Consent

- Identify next of kin for briefing.
- Family briefing should be documented in clinical notes, preferably, countersigned by participants.

Suggested Reading

Andersen LW, Granfeldt A, American Heart Association's Get with the Guidelines–Resuscitation Investigators. Association between tracheal intubation during adult in-hospital cardiac arrest and survival. JAMA. 2017;317(5):494–506. *Among adult patients with in-hospital cardiac arrest, initiation of tracheal intubation within any given minute during the first 15 minutes of resuscitation, compared with no intubation during that minute, was associated with decreased survival to hospital discharge. These findings do not support early tracheal intubation for adult in-hospital cardiac arrest*

Atkinson P, Bowra J, Milne J, et al. A P. International Federation for Emergency Medicine Consensus Statement: Sonography in hypotension and cardiac arrest (SHoC): An international consensus on the use of point of care ultrasound for undifferentiated hypotension and during cardiac arrest. CJEM. 2017;19(6):459–70. *An international consensus on sonography in hypotension and cardiac arrest*

Callaway CW, Donnino MW. Post-Cardiac Arrest Care: 2015 American Heart Association Guidelines update for cardiopulmonary resuscitation and emergency cardiovascular care. Circulation. 2015;132(18 Suppl 2):S465–82. *Current American guidelines on post-resuscitation care*

Neumar RW, Shuster M. Executive summary: 2015 American Heart Association guidelines update for cardiopulmonary resuscitation and emergency cardiovascular care. Circulation. 2015;132(18 Suppl 2):S315–67. *Current guidelines on advanced cardiac life support*

Nolan JP, Soar J. European resuscitation council and European society of intensive care medicine 2015 guidelines for post-resuscitation care 2015: Section 5 of the European Resuscitation Council Guidelines for Resuscitation 2015. Resuscitation. 2015;95:202–22. *Current European guidelines on post-resuscitation care*

Soar J, Donnino MW. 2017 international consensus on cardiopulmonary resuscitation and emergency cardiovascular care science with treatment recommendations summary. Resuscitation. 2018;133:194–206. *Treatment recommendations include the most recent cardiopulmonary resuscitation science reviewed by the International Liaison Committee on Resuscitation. This summary addresses the role of antiarrhythmic drugs in adults and children and includes the Advanced Life Support Task Force and Pediatric Task Force consensus statements, which summarize the most recent published evidence and an assessment of the quality of the evidence based on Grading of Recommendations, Assessment, Development, and Evaluation criteria*

Website.: www.aha.org

Comprehensive ICU Care

25

Deeksha Singh Tomar and Sachin Gupta

Case History:
A 52-year-old male smoker presented with high-grade fever, breathing difficulty, and decreased urine output, with cold clammy extremities. He was diagnosed with severe community-acquired pneumonia for which he was shifted to invasive mechanical ventilation after failing noninvasive support. He was sedated and given vasopressor support. He was ventilated with a lung protective strategy and was initiated on appropriate antibiotics.

Patients with multiorgan failure require aggressive intensive care management to optimize the failing organ systems. This has become possible with the availability of modern organ support systems. Management of such patients requires a systematic and multidisciplinary approach with the intention of preventing hospital-acquired infections. Comprehensive ICU care should start as soon as the patient enters the ICU and should include a tailor-made plan for each patient. Each patient should undergo a basic pattern of care plan as follows:

Step 1: Workforce Assessment

- The most critical patient should be nursed by the most experienced staff and the optimal nurse–patient ratio should be maintained as it helps in picking up the problems faster.
- The staffing to other areas like high dependency unit (HDU) and other less critical areas should be allocated based on the experience.

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- Patients should be transferred within the hospital in a timely and safe manner.
- All patients with grossly deranged physiological parameters should be accompanied by resident doctors.

Step 2: Detailed Handover

- To maintain continuity of patient care, a detailed handover should be exchanged between the doctors and the nurses.
- Handover exchange should be practiced in each shift change but not less than 2 times in 24 hours.
- A structured method of handover has been shown to critically influence the transfer of clinical information, and this process should be implemented for a smooth and correct transfer of information.
- Only 2.5% of patient information is retained in verbal handover, 85.5% is retained when using the combination of verbal and hand-written documentation, and 99% is retained when the handover is exchanged in a printed format.
- The handover process should be taken in an unhurried manner. The process should be done in the presence of a senior ICU clinician with minimum interruptions. Each handover session should last at least 25–30 minutes to cover around 10 patients.
- The ISBAR format should be maintained for all new patient handover and it is meant to increase safety in patient transfer. The components are as below:
  - Identity of the patient—age, gender, and admitting consultant
  - Situation—presenting symptoms/problems, stability of the patient, level of concern
  - Background—admitting complaints, relevant history, admission date, provisional diagnosis
  - Assessment and action—what has been done so far and assessment of the situation
  - Response and rationale—response to the interventions, what is pending to be done, investigations to be done, review by whom and why, further plan, ongoing medications, and further recommendations on management
- For patients who are known to the ICU team, ISBAR can be reduced to SAR.

Step 3: Proper History Taking, Clinical Examination, and Further Planning

- After taking handover from the previous doctor, the patient should be examined afresh and the previous history should be used as a guide, and an unbiased revaluation is needed.
- The history should be taken from the person who is aware of the previous and present medical issues of the patient. All relevant documents should be taken from the relatives to understand the trend of co-morbidities.

- After admission, the nurse should observe for any recent abnormal trends and should inform the duty doctor.
- Observe the patient for any evidence of respiratory distress, restlessness, or abnormal movements. For ventilated patients, the presence of spontaneous breathing and any patient-ventilator asynchrony should be noted.
- The patient should be examined after performing proper hand hygiene. The privacy of the patient should be respected, and curtains should be drawn before exposing the patient. For a female patient, the presence of a female nurse is mandatory before doing any examination. The conscious patient should be informed before exposing him or her. The examination should follow a sequence from head to toe.
- Examine for pallor, jaundice, clubbing, and any evidence of anasarca. Pupillary examination should be done for pupil size, reaction, symmetry, and any evidence of subconjunctival hemorrhage or exposure keratitis. Manipulation of the neck in trauma victims should be avoided and the neck should be stabilized with a cervical collar.
- Neurological assessment should be done with monitoring of the Glasgow Coma Scale (GCS).
- For intubated patients, the length of the endotracheal tube at the level of lips should be noted and it should be properly secured. The endotracheal tube cuff pressure should be checked with the help of a manometer, and it should be maintained at around 25 cm H_2O. A heated and moist exchanger (HME) should be placed at the inspiratory limb of the ventilatory circuit, and it should not be clogged. Check for any kinking of the endotracheal tube or the ventilator circuit to avoid any patient-ventilator asynchrony. For ventilated patients, the in-line closed suction apparatus should be ideally applied.
- For tracheostomized patients, the site should be examined for any bleeding or erythema or pus point. The tube should be snugly secured around the neck and the cuff pressure should be maintained.
- The suction frequency should be noted and the type of secretions should be documented.
- The placement of an orogastric or nasogastric tube should be confirmed both by chest radiology and by auscultation. Feeding should be ascertained by connecting with a feeding pump.
- The insertion site of a central venous line should be examined for any induration or a pus point to exclude local site infection. The ports of a central line should be regularly flushed if not being used and should not contain any backflow of blood. The lines should be secured with a suture and covered with a clean transparent dressing, which should be changed either when visibly soiled or every 3 days.
- The chest should be examined systematically. Proper placement of electrocardiography (ECG) leads, any visible skin changes, or dressing of intercostal tubes should be examined. Palpation for crepitus, percussion for the presence of dullness of pleural effusion or hyperresonance of pneumothorax, and auscultation for adventitious sounds should be done.
- Heart sounds and murmur should also be heard during auscultation.

- Abdomen examination should look for fullness, tenderness, visceromegaly, ascites, and bowel sounds. Also, look for stoma dressing and position of feeding jejunostomy or abdominal drains if any.
- All patients should undergo a rectal examination to look for any hemorrhoids or any other growth. Pelvic examination in females should not be ignored.
- Urinary catheter hygiene and proper fixation should be ascertained in all catheterized patients. The urinary bag should be hung above the ground and below the level of patient and catheter acquired urinary tract infection (CAUTI) bundle should be strictly followed.
- Upper extremities should be examined for radial and ulnar arterial pulses, blood pressure, and thrombophlebitis due to peripheral cannula. Radial arterial lines should be properly flushed and kept secured at all times.
- Lower extremities should be examined for edema, calf swelling, muscle strength, and proper fitting of intermittent pneumatic compression stockings. Femoral lines should be observed for any soiling or hematoma.
- Bed-bound patients should be log-rolled with the help of the nurse to examine the back. Pressure points should be palpated for any swelling or bogginess as they are the risk factors for pressure sores. Similarly, sacral sores should also be examined and documented.
- In post-operative and trauma patients, the wound or the surgical incision site should be examined for erythema, purulence, and any other palpable induration and tenderness. The drainage bags should be properly labeled and fixed on the abdomen.
- The nurse should note down the vitals on the ICU flowsheet. Heart rate, blood pressure, respiratory rate, SpO2, and temperature should be monitored for all patients, irrespective of the criticality status. ECG should be read to identify any arrhythmias.
- Check ventilator parameters—mode, FiO2, positive end-expiratory pressure (PEEP), tidal volume, pressure limit, ventilator rate, inspiratory-expiratory ratio (I:E ratio), and inspiratory flow. Minute ventilation, auto-PEEP, plateau pressure, driving pressure, lung compliance, and airway resistance should also be noted.
- All intravenous infusions should be labeled and connected.
- All advanced monitoring equipment should be noted and their reading documented.
- Intra-abdominal pressure should be monitored in patients at risk of developing abdominal compartment syndrome.
- Recent relevant investigations including hematology, biochemistry, microbiology, and imaging studies should be reviewed and the trend should be documented.
- All invasive procedures like central line insertion, hemodialysis catheter insertion, thoracocentesis, or abdominal paracentesis should be performed under bedside ultrasound guidance.
- Point of care ultrasound (POCUS) should be used to assess the fluid status of the patient and diagnose pleural effusion, consolidation, or even pneumothorax in clinically relevant situations.

- Familiarize with the ICU nursing chart and review it systematically. Examine the previous 24-hour trend and look for events and worst values.
- Cumulative fluid balance, daily fluid balance, protein, and calorie intake should be reviewed daily.
- Review the medication card daily for appropriateness of dosing and route of medications. Stop unnecessary medications whenever deemed appropriate.
- Review the referrals that have been done for the patient and incorporate important suggestions.
- In ICUs using electronic medical records, familiarize yourself with the system.
- Review the payor status of the patient.

Step 4: Participate in Multidisciplinary ICU Round

- Care of a critically ill patient involves teamwork. The typical ICU rounds in a tertiary care hospital involve the ICU in-charge, resident/trainee doctors, ICU nurse in-charge, duty nurses of each bed, physiotherapist or respiratory therapist, clinical pharmacist, ICU technician, and usually a social worker.
- These rounds comprise of detailed exchange of information about each patient among all the members and a detailed plan of the day for the patient is made and each member is allocated their role. These rounds put emphasis on physiological derangements rather than admitting diagnosis. These rounds aim to stabilize the patient to a non-critical state so that they can be transferred to a lower level of care from the ICU.
- These rounds are also being used for bedside training of younger colleagues and trainees in the team.
- The treatment plan should take into account all organ systems of the patient, such as neurological (assessment of sedation and analgesia), respiratory, cardiovascular, renal, metabolic (including nutrition planning), hematological, and gastrointestinal. Special emphasis should be placed on infection control practices that are required for the patient and appropriate antibiotics should be initiated if required. ICU rounds are conducted in a smooth and coordinated manner if all the members speak the same terminologies and understand the patient (Table 25.1).
- Each patient handover should start with the identification of the patient including name and gender followed by the day of ICU stay, reason for admission, and significant past history. Then any significant event in the previous 24-hour period should be highlighted.
- A brief mention of patient vitals, various organ-specific investigations and examination findings, the presence of invasive lines, and medications initiated should be mentioned. Areas of major concern should be addressed and the treatment plan and goal should be elaborated. Each patient case presentation should be short and precise and should not take more than 5 minutes.

Table 25.1 Outcome and process variables

System	Outcome variables	Process variables
Neurological	Glasgow coma scale (GCS) Motor function Sedation score Agitation level (delirium) Pain level Occurrence of seizures Intracranial pressure	Type/route of antipsychotic medications Type/route of analgesics Type/route of sedatives Type/route of anti-epileptics Intracranial pressure monitors
Pulmonary	Oxygen saturation Chest x-ray findings Presence of crepitations or wheeze Arterial blood gas analysis Spontaneous ventilation rate in intubated patients Compliance and resistance of airway	Supplementation of oxygen Administration of nebulized bronchodilators Ventilator settings Daily assessment of the readiness of weaning and extubation criteria Need for antibiotics or pleural fluid tapping based on chest x-ray
Cardiovascular	Blood pressure Heart rate Abnormal cardiac rhythm Presence of crepitations Peripheral pulses Warmth of the limbs Evidence of myocardial ischemia on ECG Cardiac output noninvasively or invasively	Estimation of preload either by inferior vena cava assessment or more dynamic indices or continuous central venous pressure monitoring Estimation of afterload and therapy by vasodilators Adjustment of anti-arrhythmic agents based on either drug level or toxicity on ECG Titration of vasopressors or antihypertensives to keep optimum mean arterial pressure (MAP)
Renal	Weight of the patient Blood urea nitrogen and serum creatinine Arterial blood gas (ABG) analysis Electrolytes Urine output Net intake/output balance	Correction of metabolic acidosis in ABG Supplementation of electrolytes Intravenous fluid composition and rate Sites of unexpected loss of specific electrolytes
Gastrointestinal/ metabolic/nutrition	Bowel sounds and function Tolerance of enteral feeds Fraction of daily calorie target achieved Hypo/hyperglycemic events Nitrogen balance	Need for prokinetic or antiemetic agents Route/rate/composition of enteral feeds Prophylaxis against gastrointestinal bleeding Insulin requirement Hormone therapy like for thyroid disorders

(continued)

Table 25.1 (continued)

System	Outcome variables	Process variables
Hematologic	Findings suggestive of new episodes of bleeding Hematocrit, platelet count, and coagulation parameters Existent liver disorder	Transfusion requirement Deep venous thrombosis prophylaxis
Infectious disease	New onset fever Features suggestive of infectious issues Presence of organisms on gram stain and various cultures Leucocyte count and differential count Raised biomarkers	Investigations to diagnose fever Steps to prevent infection Appropriate antimicrobial prescription Follow antimicrobial stewardship

Adapted from www.sccm.org
Medical students' guide to intensive care medicine

Step 5: Documentation in Clinical Notes

- Documentation should be done in a detailed manner highlighting the current clinical condition of the patient as well as the treatment plan for areas of concern.
- Appropriate clinical notes can give entire information about the patient on a daily basis and are the most important document of the patient file. The patient notes can be either put in the patient's file or electronic depending upon the institute's protocol. All clinical notes should contain the date, time, name, signature, and employee ID of the person who is documenting them.
- The SOAP (subjective, objective, assessment, plan) format may be utilized in clinical notes for short-stay cases. *Subjective* includes patient's complaints, history of present illness, past medical history, and general review of various organ systems. *The objective* includes vital signs, physical examination findings, and various investigation data. *Assessment* includes forming a differential diagnosis after evaluating the problems of the patient. *The plan* includes advice for further testing and additional consultation with other specialties to mitigate the problems.
- For long-stay cases, a more detailed and comprehensive checklist should be incorporated to address all major concerns of the patient (Table 25.2).
- There should be a continuous quality improvement project that should be undertaken in the ICU in an attempt to improve patient outcomes (Table 25.3).
- Family briefing and communication should be documented daily. The surrogate or representative of the patient should be educated on it and made to sign which acts as a proof that the condition of the patient has been updated to the family.

Table 25.2 Daily checklist

Daily variable
F = Feeding
A = Analgesia
S = Sedation
T = Thromboprophylaxis
H = Head end elevation
U = Ulcer prophylaxis
G = Glycemic control
S = Spontaneous breathing trial
B = Bowel movement
I = Indwelling catheter
D = Drug de-escalation

Table 25.3 Continuous quality improvement (CQI) checklist

What needs to be done to reduce ICU length of stay?
What are the greatest risks for the patient in the ICU, and what steps can be taken to reduce them?
What methods to follow to reduce pain in critically ill patients?
How to optimize cardiac output in ICU patients?
How to ensure lung protective ventilation strategies for all patients?
FASTHUGSBID for all patients
Early mobilization for all patients
Methods to reduce hospital-acquired infections in ICU patients
How to improve feeding tolerance and ensure proper nutrition
Plan de-escalation of drugs on a daily basis if possible
Order clinically justifiable tests and procedures
Review the trend of morning investigations
Can catheters be removed from the patient?
Effective communication with the family
Continuous update to the admitting consultant

Step 6: Perform the Procedure Under Supervision

- Each doctor in the ICU team should acquire the technical skills required to perform various procedures in the ICU.
- During the training period, one should be able to understand the indications, contraindications, anatomy, steps of the procedure, use of ultrasound for real-time procedure, and complications of the procedure.
- The trainees should first observe the procedure being done by the seniors and get familiarized with various aspects of the technique.
- All elective procedures should be preceded by informed written consent either by the patient (if conscious) or by the next of kin or legally authorized representative of the patient.
- One should be aware of when not to do a procedure or abandon a procedure as “do no harm” should be the motto.
- Post-completion, the procedure should be documented in the patient notes and complications if any should also be mentioned.

Step 7: Implement Infection Control Practices

- Take leadership and exemplary role in maintaining proper infection control practices in your unit.
- Teaching infection control practices to juniors and other consultants visiting the ICU should be practiced continuously. Similar training should be given to ancillary personnel involved in the care of the patient like physiotherapists, housekeeping services, technicians, etc.
- All nosocomial infections should be immediately reported and steps should be taken to prevent further infections.
- Antimicrobial stewardship should be practiced.
- All invasive procedures should follow the basic steps of infection control like cleaning and draping of the site as well as the proper surgical washing of the hands of the person who is doing the procedure.
- Patients requiring isolation in ICU should be identified early and should be shifted to isolation rooms. The pressure within these rooms should be adjusted to positive or negative depending upon the condition for which they have been isolated.

Step 8: Counsel Family Members

- Family counseling is an art, and it should be learned by observing your seniors speaking to the family members.
- Listening to the family in detail is the key to non-conflict during family counseling. Be truthful in updating the clinical condition of the patient and also in sharing your expectations regarding the clinical path of the patient with the family members.
- Do not fall into an argumentative discussion with the family members.
- End-of-life issues should ideally be discussed by a senior member of the ICU team as it is a very sensitive issue.
- Above all, be compassionate in all family counseling meetings.

Step 9: Contribute to the Activities of the ICU Team

- Each member of the ICU team has a defined role and this is the basis of teamwork.
- Effective communication is very important among team members as many of the tasks performed in the ICU are interdependent.
- Each member should be aware of all policies and protocols of the ICU as they may be different from your previous work experience.
- Create a safe work culture, avoid distractions, and keep the ICU environment clean, calm, and acceptable to patients and family members.

- The basics of workplace ethics like punctuality, a defined dress code (maybe scrubs), keeping ICU noise low, respect for all members working in the ICU, and proper mannerisms should be always followed.
- Be updated with the latest scientific literature related to your work and attend departmental scientific meetings regularly.
- Take active participation in various quality audits being conducted in the ICU.
- Always clear your doubts about any aspect of ICU working with your seniors.

Step 10: Keep Yourself Updated

- Actively participate in academic and research activities in the ICU.
- Try to lead a research topic that can improve patient care in the ICU.
- Read the latest literature to stay abreast and try following a reference book or handbook for quick revision.
- Be updated regarding the hospital drug formulary and always refer to it for any doubts about drug dosing.
- Always have a valid Advanced Cardiac Life Support (ACLS) certificate while working in the ICU.
- One should have basic training in using Point-of-care Ultrasound (POCUS) for various procedures, assessment of fluid status, lung ultrasound, and basic echocardiography.
- Attend simulation-based training courses to understand and develop procedural skills.
- Try becoming a member of a professional society for various workshops, conferences, and CME.
- Try completing the syllabus during your training period and try completing the course in which you have been enrolled.
- Try becoming a senior member of the team once a new junior colleague joins and helps them in their journey.

Suggested Reading

CoBaTrICE Collaboration, Bion JF, Barrett H. Development of core competencies for an international training programme in intensive care medicine. Intensive Care Med. 2006;32(9):1371–83. *Defines the core (minimum) competencies required for a specialist in adult intensive care medicine*

Dorman T, Angood PB. Guidelines for critical care medicine training and continuing medical education. Crit Care Med. 2004;32(1):263–72. *Guidelines for the continuum of education in critical care medicine from residency through specialty training and ongoing throughout practice*

Dubosky MN, Chen YF. Vibrating mesh nebulizer compared with metered-dose inhaler in mechanically ventilated subjects. Respir Care. 2017;62(4):391–5. *No association was found between an MDI or vibrating mesh nebulizer and our primary outcomes, days receiving ventilation, in-hospital mortality, or VAP, in mechanically ventilated subjects*

Gogineni H, Aranda JP, Garavalia LS. Designing professional program instruction to align with students' cognitive processing. Curr Pharm Teach Learn. 2019;11(2):160–5. https://doi.org/10.1016/j.cptl.2018.11.015. Epub 2019 Jan 3. PMID: 30733012.

Nanchal R, Aebly B, Controlled trial to improve resident sign-out in a medical intensive care unit. BMJ Qual Saf. 2017;26(12):987–92. *A structured sign-out process compared with usual sign-out significantly reduced the occurrence of non-routine events in an academic MICU*

Pronovost P, et al. Improving communication in the ICU using daily goals. J Crit Care. 2003a;18(2):71–5.

Pronovost P, Weast B, Schwarz M, Wyskiel RM, Prow D, Milanovich SN, Berenholtz S, Dorman T, Lipsett P. Medication reconciliation: a practical tool to reduce the risk of medication errors. J Crit Care. 2003b;18(4):201–5. https://doi.org/10.1016/j.jcrc.2003.10.001. PMID: 14691892.

Thompson JE, Collett LW. Using the ISBAR handover tool in junior medical officer handover: a study in an Australian tertiary hospital. Postgrad Med J. 2011;87(1027):340–4. *Use of the ISBAR tool improves JMO's perception of handover communication in a time-neutral fashion*

Vanhanen M, Meriläinen MH, Ala-Kokko T, Kyngäs H, Kaakinen P. Family members' perceptions of counselling during visits to loved ones in an adult ICU. Nurs Open. 2023;10(7):4859–67. https://doi.org/10.1002/nop2.1738. Epub 2023 Apr 5. PMID: 37018387; PMCID: PMC10277426.

Vincent JL. Give your patient a fast hug (at least) once a day. Crit Care Med. 2005;33:1225–9. *A check list for ICU processes*

Wibrandt I, Lippert A. Improving patient safety in handover from intensive care unit to general ward: A systematic review. J Patient Saf. 2017. *Well-conducted study on this important topic. Giving patients and their families a supplementary written or verbal status report before transfer might improve patient safety. The introduction of a Liaison Nurse may be effective in improving communication between ICU and ward staff, which might reduce risks in patient safety. However, there is no evidence of improved mortality and/or readmission rates after introducing handover tools in the transfer from the ICU to the ward*

Website

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Sedation, Analgesia, and Paralysis in ICU

26

Sunil Karanth, Ranveer Tyagi, and M. Padyana

Case Vignette

A 40-year-old gentleman with no known comorbidities presented with acute onset of abdominal pain lasting for 5 days. On evaluation in the Emergency Department, he was found to be tachycardic with a heart rate of 140/minute, tachypneic with a respiratory rate of 40/minute saturating 85% on room air, and a blood pressure of 100/60 mm Hg. Systemic examination revealed abdominal tenderness in the epigastric region. A blood gas analysis revealed lactate of 4 mmol/L. He was started on oxygen supprt through face mask and administered a stat dose of fentanyl for analgesia. Following initial resuscitation, he showed some respite in terms of improvement in pain score and a decrease in the heart rate to around 130/min. A contrast CT abdomen with pelvis was performed, which showed a bulky edematous pancreas suggestive of acute pancreatitis. He was transferred to the ICU for further care. In view of ARDS, he was commenced on high-flow nasal cannula (HFNC) and patient-controlled analgesia with fentanyl. Over the next 24 hours, despite HFNC, he had worsening respiratory distress needing to be intubated with modified rapid sequence induction. Post-intubation, in view of a poor PaO2/FiO2 ratio, he was kept deeply sedated and paralyzed to facilitate proning. After a session of proning, he improved and, over the next 48 hours, was weaned off paralysis and sedation. However, on day 4 of ICU admission, he developed ICU delirium. He was commenced on a dexmedetomidine infusion, which improved his condition. He was weaned off the ventilator and extubated successfully on day 6 of admission. Fentanyl PCA was provided for analgesia, and he was transferred to the wards the next day.

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A critically ill patient admitted to the intensive care unit (ICU) experiences various unpleasant stimuli in the ICU due to a variety of factors that may be related to the underlying illness, secondary to uncontrolled light and noise, etc. Besides, many patients commonly experience pain even at rest, while additional pain and discomfort could occur consequent to providing general care procedures or when subjected to various invasive procedures. This type of severe or poorly controlled pain may induce a stress response in critically ICU patients causing disturbed sleep, delirium, and agitation resulting in both short-term and long-term consequences

- Short-term effects include sympathetic stimulation, which causes impaired tissue perfusion, increased myocardial oxygen consumption, hyperstimulation of catabolism leading to hyperglycemia, breakdown of muscle, lipolysis, and even impaired wound healing.
- Long-term consequences may be depression, anxiety, and chronic pain syndromes.

  Deep sedation and delirium are associated with increased length of stay in ICU, on the ventilator, and also in mortality. The 2018 Pain, Agitation/Sedation, Delirium, Immobility (rehabilitation/mobilization) and Sleep (disruption) (PADIS) guidelines provide an evidence-based approach to meet these goals.

Step 1: Assess the Need for Analgesia

- Evaluation starts with the assessment of pain, which becomes an important first step in the management.
- This sensation is highly individualized in nature needing a personalized approach to every patient. Factors to be considered in assessing pain and its effects include:
  - Intensity of pain experienced
    - Involves a component of subjectiveness and the ability to endure the pain
  - Source of origin (including neuropathic, visceral, and somatic causes)
  - Presence of compounding factors like anxiety and depression
  - Demographic factors (young age, Caucasian race, female gender)
  - Comorbidities
  - Previous procedures
  - Barriers to assessment:
    - Communication disorders
    - Altered mental status
    - Mechanical ventilation
    - Invasive procedures and devices
    - Immobility
  - An assessment-driven, standardized pain management is quintessential
    - This approach is associated with reduced nosocomial infections, reduced risk of hypotension, bradycardia, and other secondary outcomes such as duration of ventilation and ICU stay.
    - Pain assessment with the use of validated reproducible tools

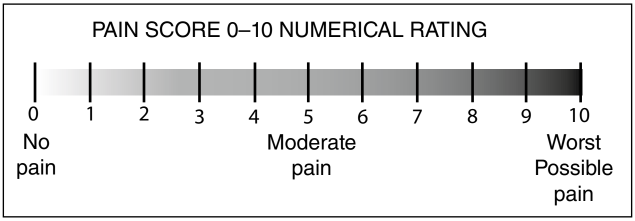
PAIN SCORE 0–10 NUMERICAL RATING
0
1
2
3
4
5
6
7
8
9
10
No pain
Moderate pain
Worst Possible pain

Fig. 26.1 Numerical rating scale (NRS) for awake patients. Scores range from 0 (no pain) to 10 (maximum pain)

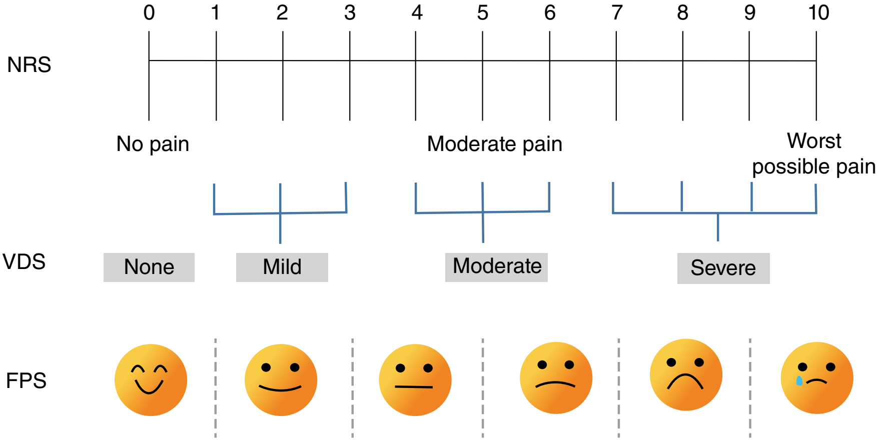
NRS
0
1
2
3
4
5
6
7
8
9
10
No pain
Moderate pain
Worst possible pain
VDS
None
Mild
Moderate
Severe
FPS

Fig. 26.2 Comparison of different pain assessment scales: numeric rating scale (NRS), verbal descriptor scale (VDS), and faces pain scale (FPS)

- Patients who are able to self-report the 0–10 Numeric Rating Scale (NRS) (Fig. 26.1) are recommended for pain assessment. A score of less than 3 on NRS would indicate adequate analgesia, while 10 would indicate the worst pain experienced by the patient.
- The Verbal Descriptor Scale (VDS) is a more descriptive form of pain assessment scale where a string of descriptive words and phrases are used to refer to various intensities of pain with a horizontal line 10 cm long indicating “no pain,” “very severe pain,” or “extremely severe pain” at each end (Fig. 26.2). It can be used on ICU patients on whom numerical scales cannot be used.
- For patients who cannot self-report the assessment tools that can be used are the Behavioral Pain Scales (BPS) (Table 26.1) and the Critical-Care Pain Observation Tool (CPOT) (Table 26.2). These two systems show the greatest validity and reliability for monitoring pain. The family can participate in the patient’s pain assessment in these situations. Though the family-reported pain is closer to the patient’s self-reported

Table 26.1 Behavioral pain scale (BPS) score —from 3 (no pain) to 12 (maximum pain)

Facial expression	Relaxed	1
	Partially tightened (e.g., brow lowering)	2
	Fully tightened (e.g., eyelid closing)	3
	Grimacing	4
Upper limb	No movement	1
	Partially bent	2
	Fully bent with finger flexion	3
	Permanently retracted	4
Compliance with ventilation	Tolerating movement	1
	Coughing but tolerating ventilation most of the time	2
	Fighting ventilator	3
	Unable to control ventilation	4

Table 26.2 The critical care pain observation tool (CPOT) score—from 0 to 8 and the target is 0 to 1

1	Facial expression	Relaxed, neutral	0
		Tense	1
		Grimacing	2
2	Body movements	Absence of movement or normal position	0
		Protection	1
		Restlessness	2
3	Muscle tension	Relaxed	0
		Tense, rigid	1
		Very tense or rigid	2
4	Compliance with ventilator (intubated patients) *OR* Vocalization (extubated patients)	Tolerating the ventilator or movement	0
		Coughing but tolerating	1
		Fighting the ventilator	2
		Talking in a normal tone or no sound	0
		Sighing or moaning	1
		Crying out, sobbing	2

pain as compared to the assessment by healthcare workers, there was a general tendency by the family to overestimate the pain.

- The use of vital signs like heart rate, blood pressure, respiratory rate, oxygen saturation, and end-tidal CO_2 are not reliable for pain monitoring and assessment in such ICU patients.

Step 2: Manage Pain

- Guidelines for medication selection and dosage in a step-by-step approach, prioritizing pain control over sedation, are preferable—called the "analgesia-first approach."
  - Optimize nonpharmacologic measures like improving patients' comfort, maintaining a proper body posture, fixation of fractures, removal of any other

physical stimuli, etc. This helps treat the source of the noxious stimuli, reducing the need for unnecessary analgesia.

- Choosing the right analgesia (Table 26.3):
  - Various pain-modulating medications such as opioids, non-steroidal anti-inflammatory drugs (NSAIDs), paracetamol, and anticonvulsants are available.
  - Select the right analgesic with the optimal dose.
  - Choice and dose will be dependent on the type of pain, intensity of pain, PK/PD characteristics of the drugs, clinical profile, and organ dysfunctions at the time of administration.
  - Intravenous opioids are generally preferred front-line analgesics for non-neuropathic pain. Commonly used opioids include fentanyl, morphine, hydromorphone, and more recently remifentanil.
  - Non-opioids used as adjuncts in a "multi-modal analgesia" strategy are employed to reduce the dose of opioids and augment the pain-modulating effects, improving overall outcomes. The most commonly used adjuncts with opioids include paracetamol and ketorolac (non-cox-2 inhibitor), which can help reduce the dose of opioids by 25–50%.
  - Low-dose ketamine has also been used as an adjunct for analgesia in ICU patients.
  - Neuropathic pain is managed by using analgesics such as gabapentin, carbamazepine, and pregabalin along with an opioid.
  - COX-1-selective NSAIDs should not be routinely used as adjuncts in ICU patients.
- Dosing of analgesics*:* As a generally accepted strategy, analgesics are administered as a continuous IV infusion unless contraindicated. This helps maintain a steady serum concentration and dose titration. Continuous infusion also decreases the need for boluses, which could be fraught with the risk of adverse effects due to the need for a larger dose of medication.
- As an alternative option, patient-controlled analgesia (PCA) can be used where the analgesic is administered upon the patient's need delivered by a patient-controlled pump delivering a bolus dose of medication.
- A transdermal route of delivery, particularly a fentanyl patch, can be used for long-term analgesia, although the degree of absorption varies according to permeability, body temperature, tissue perfusion, and skin thickness. The patch takes 12 to 24 hours to reach maximal effectiveness; it is not recommended for rapid pain control.

Table 26.3 Drug details for sedation and analgesia

Drug	Time to onset (min)	Duration of effect of one dose (h)	Presence of active metabolites	Accumulation in renal failure	Dose (IV)	Comments
Fentanyl	1–2	2–4	No	No	B = 50–100 mcg	Reduces tachypnea
						Respiratory depression
					I = 0.7–10 mcg/kg/hr	Accumulation in hepatic/renal failure
Morphine	5–10	2–4	Yes	Yes	B = 1–10 mg	Same as other opioids
					I = 2–10 mg/h	
Remifentanil	1–2	10–20 mt	No	No	B = 1 mcg/kg	Decreased heart rate and blood pressure
					I = 0.25–1.0 mcg/kg/min	Increased intracranial pressure
Hydromorphone	5–10	2–4	Yes	Yes	B = 0.2–0.6 mg	May work in patients tolerant to morphine and fentanyl, respiratory depression
					I = 0.5–3 mg/h	Highly addictive
Lorazepam	5–20	6–8	No	Yes	B = 2–4 mg	Propylene glycol toxicity (anion gap metabolic acidosis, renal insufficiency)
					2–6 mg q4 to q6 (duration too long for effective infusions)	Independent risk factor for delirium
Midazolam	2–10	1–4	Yes	Yes	B = 2–5 mg	Many drug interactions
					I = 1–20 mg/h	May increase midazolam levels
Propofol	30–50 s	3–10 (dose dependent)	No	Insignificant	B = 0.2–2 mg/kg (maximum 20 mg)	Hypotension
						Increased serum triglyceride
					I = 10–150 mcg/kg/min	Propofol infusion syndrome (>5 mg/kg/h for more than 48 h)
Dexmedetomidine	30	4	No	No	B = 1 µg/kg (should be given over 15–20 min)	Sedative, anxiolysis, with analgesic property (reduces opioid requirement by >50%)
					I = 0.2–0.7 µg/kg/h	Notable adverse event is bradycardia

B - bolus; *I* - infusion

Step 3: Reevaluate the Responses to the Treatment Using the Same Pain Assessment Tools

The response to the treatment of pain is evaluated by using the pain assessment tools again and deciding about increasing the dose or adding sedation.

Step 4: Assess the Need for Sedation—Beyond Analgesia

Indications of sedation and analgesia are described in Table 26.4.

- After pain management sedation is added to achieve the goals.
- Unless there's a clinical need, the optimal sedation will be light sedation—enough to keep the patient asleep, but easily arousable with maintenance of the sleep-wake cycle. Deep sedation with or without paralysis is sometimes needed in special situations depending on the clinical need.
- There are various sedation assessment tools, including the RASS, Ramsay scale, Riker SAS, Motor Activity Assessment Scale (MAAS), and Observer Assessment of Alertness/Sedation (OAA/S) scale. Among them, the RAAS (Table 26.5) and Riker SAS (Table 26.6) are widely used to assess the degree and depth of sedation in ICU patients.

Table 26.4 Indications of sedation and analgesia

Facilitation of endotracheal intubation and mechanical ventilation (for amnesia, anxiolysis, reduction of agitation, toleration of endotracheal tube (ETT) and to reduce cough, to alleviate dyspnea, to minimize pain, and to prevent self-extubation)
While performing invasive procedures
To facilitate nursing care
Postoperative/trauma pain
To tolerate ICU environmental influences (stressful environment, monitoring devices, noise, fear of illness, separation from family)
During severe hypoxemia to tolerate certain ventilatory strategies (low tidal volume ventilation, high-frequency oscillation (HFO), and prone positioning)

Table 26.5 Richmond agitation-sedation scale (RASS) (target 0 to −3)

Combative, violent, danger to staff	+4
Pulls or removes tubes or catheters, aggressive	+3
Frequent nonpurposeful movement, fights the ventilator	+2
Anxious, apprehensive, but not aggressive	+1
Alert and calm	0
Awakens to voice (eye opening/contact) >10 s	−1
Light sedation, briefly awakens to voice (eye opening/contact) <10 s	−2
Moderate sedation, movement or eye opening (no eye contact)	−3
Deep sedation, no response to voice, but movement or eye opening to physical stimulation	−4
Unarousable, no response to voice or physical stimulation	−5

Table 26.6 Riker sedation-agitation scale (SAS) (target sedation 3 to 4)

Dangerous agitation, pulling the ETT, trying to remove catheters, climbing over bedrail, striking at staff, thrashing side to side	7
Very agitated, requiring restraint and frequent verbal reminding of limits, biting the ETT	6
Agitated, anxious or physically agitated, calms to verbal instructions	5
Calm and cooperative easily arousable, follows commands	4
Sedated, difficult to arouse but awakens to verbal stimuli or gentle shaking, follows simple commands but drifts off again	3
Very sedated, arouses to physical stimuli but does not communicate or follow commands, may move spontaneously	2
Unarousable, minimal or no response to noxious stimuli, does not communicate or follow commands	1

- It is generally accepted to classify the depth of sedation as light, moderate, or deep, where light sedation usually ranged from −1 to −2 on the Richmond Agitation-Sedation Scale (RASS) in most studies as against a RASS score of −2 to +1 in a few other studies.
- A light level of sedation can be achieved and maintained using daily sedation interruption (DSI) and nurse-protocolized targeted sedation protocol (NP-targeted sedation).
- NP-targeted sedation is applied by nurses who titrate drug doses at the bedside to achieve the targeted sedation score.
- Following a structured assessment, continuous infusion dosing is recommended where it's practical and possible to achieve the necessary sedation targets. If not alternatively, less preferred intermittent dosing can be used.
- In those patients where a sedation scale cannot be used due to the need for deep sedation or the use of a neuromuscular blocker, the depth of sedation can be monitored using objective methods such as bispectral index (BIS) monitoring and auditory evoked potentials.
- Frequent reevaluation and readjustment of sedation targets may be needed from time to time.

Choose a Drug for Sedation

- Based on indications, goals, clinical pharmacology, organ dysfunctions, and other factors.
- A sedative with rapid onset and offset of action is preferred. The choice of sedation is largely met by propofol and dexmedetomidine. Benzodiazepines which used to be the cornerstone of therapy as a sedative-hypnotic are preferred only for alcohol withdrawal syndrome.
  - Benzodiazepines:
    - For anterograde amnesia.
    - Eliminates memory of unpleasant experiences that occur following drug use.

    - Anticonvulsant effect, but no analgesic action. Their main indications for use in the ICU include sedative treatment and short-term use for anxiety, alcohol withdrawal, preoperative anxiety, initial treatment of convulsions, muscle spasms, and insomnia. The risk of prolonged action and accumulation is higher after using a prolonged infusion, elderly, renal, and hepatic dysfunction.
  - Propofol:
    - For general anesthesia and sedation.
    - Sedative, sleep-inducing, anti-anxiety, memory loss, antiemetic, and anticonvulsant effects, but no analgesic effect, found to reduce cerebral blood flow and brain metabolism.
    - There's no need for any pharmacokinetic changes in patients with renal or hepatic failure. Due to the rapid clearance of its sedative effect, temporary discontinuation during infusion allows a neurological evaluation.
  - Dexmedetomidine:
    - Selective α2-agonist and has sedative, analgesic, and sympathetic suppression effects with less respiratory depression as compared to other sedatives.
    - Sedation similar to that of normal physiological sleep.

Step 5: Assess the Need for the Use of Neuromuscular Blockade (NMBA)

- *Indications for use of NMBA in ICU*
  - Rapid sequence intubation (RSI): The most commonly used NMBA are succinylcholine and rocuronium.
  - Acute respiratory distress syndrome (ARDS):
    - Facilitates lung protective ventilation by preventing the start of spontaneous respiratory efforts, and helps decrease the work of breathing consequentially reducing oxygen consumption by abolishing resting muscle tone.
    - Helps improve chest wall compliance, reduce patient-ventilator asynchrony, facilitate lung recruitment, and reduce the inflammatory response of ARDS.
    - NMBA as a continuous infusion with cisatracurium in patients with moderate to severe ARDS showed improvement in mortality in one of the studies, but no benefit in a more recent trial. Recent RCT showed neither benefit nor harm. Re-evaluation of the Systemic Early Neuromuscular Blockade (ROSE) study showed that the use of cisatracurium infusion for 48 hours, compared with its intermittent administration in patients with ARDS, resulted in no significant differences in mortality. The current recommendation is that NMB may be considered if clinically indicated in severe ARDS.

- Status asthmaticus: To facilitate synchrony with the ventilator, prevent excessive hyperinflation, help reduce airway pressures, and decrease the activity of the respiratory muscles.
- Reduction of Intracranial pressure (ICP): Helps in the reduction of carbon dioxide, reduces positive end-expiratory pressure, decreases metabolic output, and limits ICP surges after stimuli such as tracheal suctioning, coughing, movement, agitation, and postural changes.
- Elevated intra-abdominal pressure (IAP).
- Therapeutic hypothermia after cardiac arrest.

Step 6: Choose Neuromuscular Blockade and Monitor Its Effects in the ICU (Table 26.7)

- NMBA are classified according to their mechanism of inducing neuromuscular blockade.
  (a) Depolarizing agents, including succinylcholine: The rapid effect and 3- to 5-minute duration of succinylcholine make it useful in short procedures, such as orotracheal intubation.
  (b) Non-depolarizing agents are further classified as
    - Aminosteroids (such as rocuronium, vecuronium, and pancuronium), which undergo hepatic metabolism and renal elimination to varying degrees depending on the drug.
    - Benzylisoquinolines (including cisatracurium and atracurium) metabolized at physiological pH through Hoffmann elimination (an organ-independent mechanism).

Table 26.7 Neuromuscular blocking agents commonly used in the ICU

Type	Agent	SD 95/intubation dose (mg/kg)	Start time (Minutes)	Infusion dose (ug/kg/minute)	Duration of action (minutes)
Depolarizing	Succinylcholine	0.5–0.6/1–1.2	<I	NF	10–12
Non-depolarizing: Aminosteroids	Rocuronium	0.3/0.6 (1.2 for fast sequence induction)	1.5–3 (I for rapid induction dose)	5–12	20–70
Non-depolarizing: Aminosteroids	Pancuronium	0.07/0.1	3–5	0.8–1.7	20–40
Non-depolarizing: aminosteroids	Vecuronium	0.05/0.08–0.1	3–5	0.8–1.7	20–40
Non-depolarizing: benzylisoquinolines	Cisatracurium	0.05–0.07/0.15	4–7	1–3	35–50
Non-depolarizing: benzylisoquinolines	Atracurium	0.4/0.4–0.5	3–5	5–20	20–35

- *Monitoring the level of NMB*
  - Titration of neuromuscular blockade is best done by the use of neuromuscular transmission monitoring.
  - Quantitative monitoring methods are ideal, but cumbersome at the bedside.
  - Qualitative methods are more practical.
  - Principle: Stimulation of peripheral nerves while recording, quantifying, and numerically displaying the evoked response patterns.
  - Many available techniques.
  - All these devices perform various patterns of neurostimulation; they include train of four (TOF), single contraction, double burst, and post-tetanic potentiation count (PTC).
  - Most widely used method of NMT monitoring through peripheral nerve stimulation by TOF.
  - Ensures an appropriate level of blockade and decreases the total dose of NMBA administered.
  - Train of four (TOF):
    - Administration of four supramaximal stimuli for 0.5 s (2 Hz).
    - Repeated every time the evaluation of neuromuscular relaxation is needed.
    - The repetitive stimulus produced by the four contractions in a row produces a decrease in the muscular response and constitutes the basis of the evaluation in such a way that the ratio of the amplitude of the fourth contraction to the first provides the TOF value. When there is no effect of any neuromuscular relaxant, the TOF value is equal to 1 (100%), and in conditions of partial NMB, the TOF value is inversely proportional to the level of blockade.
  - Discontinuation of NMB has to be considered at the earliest possible opportunity when the patient is clinically ready for it. Cessation of NMB with continuing deep sedation or a TOF-guided cessation of NMB can be considered.
  - Due to an inability to assess sedation underneath paralysis, DO NOT wean down sedation unless the paralytics are interrupted and have worn off. Sedative and analgesic continuous infusion doses that achieved pre-paralysis RASS −4/−5 should be maintained throughout this period.

Step 7: Daily Interruption of Sedation and Reassess Its Need

- The critically ill patients often have deranged hepatic and renal function leading to prolonged metabolism of medications used.
- Daily sedation interruption (DSI) helps give time for the accumulated sedative/analgesic drugs to metabolize, with resultant patient arousal and facilitation of neurological status assessment in some patients. This strategy along with a spontaneous breathing trial (SBT) has been shown to decrease the duration of mechanical ventilation, ICU, and hospital stay.

- The patient should not be left unattended after the sedation is stopped. This should be done in the morning hours, when there is better staffing, to avoid any tubes or lines from being pulled out by the patient.
- In critically ill, intubated adults either DSI protocols or nurse-targeted sedation can be used to achieve and maintain a light level of sedation. If a nurse-targeted sedation is able to achieve lighter levels of sedation, DSI is not required.

Step 8: Discontinuation of Sedation

- This step may often be an extension of DSI.
- All those patients who are on sedation infusion for over a week are at risk of developing withdrawal symptoms manifested as neurological changes or physiological dependence—especially if abruptly discontinued. This can be prevented by lowering the sustained infusion rate by 20–40% for the first time, with an additional 10% reduction every 12–24 hours depending on the patient's response.

Step 9: Prevent, Assess, and Treat Delirium

- Delirium is defined as acute cerebral dysfunction accompanied by a change in the level of consciousness, disorientation, and cognitive dysfunction during a short duration (hours to days).
- Delirium is classified into three subtypes:
  1. Hyperactive (agitated)
  2. Hypoactive (calm or lethargic)—associated with a poorer prognosis
  3. Mixed (fluctuation between the two subtypes)—most common
- 20% to 80% of critically ill adult patients have experienced delirium during their ICU stay.
- The PREdiction of DELIRium in ICu patients (PRE-DELIRIC) model and early (E)-PRE-DELIRIC model can predict delirium in critically ill adult patients.
- Delirium is associated with poorer short- and long-term outcomes.
  - Short term: Increased mortality, longer ICU and hospital stay, higher healthcare costs.
  - Greater long-term cognitive dysfunction such as dementia.
  - Prevention of risk factors (Table 26.8), early recognition, and treatment are associated with a good outcome.
- Thus, adult ICU patients should be routinely evaluated for delirium using a validated tool.
- The CAM-ICU (Fig. 26.3) and ICDSC (Table 26.9) are the most widely used and validated. Patients with an RASS score > −4 or SAS score > 2 would be the first prerequisite to make them eligible for delirium evaluation using the CAM-ICU. Ideally, clinicians should perform the CAM-ICU at least twice a day (day and night) to assess delirium.

Table 26.8 Risk factors for delirium

Use of benzodiazepines
History of hypertension
Transfusion
Increasing age
Prior dementia
Pre-ICU emergency operation
Admission because of a neurologic disease
Trauma
Use of psychoactive medication
Prior coma, increasing APACHE and ASA scores

- *Pharmacologic prevention and treatment of delirium*:
  - Pharmacologic agents used for the treatment of delirium include the following:
    - A typical antipsychotic like haloperidol
    - Atypical antipsychotics like risperidone, olanzapine, and quetiapine
    - Dexmedetomidine
  - The short-duration use of haloperidol or an atypical antipsychotic may be helpful for patients who experience significant distress secondary to delirium or may be at risk of causing physical harm to themselves or others. Atypical antipsychotics are preferred as they have a lower risk of extrapyramidal symptoms than haloperidol; however, atypical antipsychotics are not recommended for use in patients at risk of torsades de pointes (as in those with a prolonged QT interval, administration of drugs that prolong the QT interval, or a history of arrhythmias).
  - Dexmedetomidine use may also be considered in patients with delirium on mechanical ventilation. Although benzodiazepines are known to induce delirium, they can be used in patients with secondary delirium related to alcohol or benzodiazepine withdrawal.
  - The use of haloperidol or an atypical antipsychotic in patients with subsyndromal delirium is not associated with a reduced incidence of delirium or an improved prognosis.
  - There is no role for any of the drugs in the prevention of delirium.
- *Nonpharmacologic prevention and treatment:*
  - The multicomponent interventions may include the following:
    - Performing reorientation
    - Stimulating cognitive capability
    - Using clocks
    - Improving sleep quality by minimizing light and noise
    - Minimizing sedation
    - Reducing immobility through early rehabilitation and exercise
    - Decreasing hearing and/or visual impairment by using available devices including hearing aids or eyeglasses
  - The increase in compliance with the ABCDEF bundle (ICU LIBERATION BUNDLE) is significantly related to decreased mortality and prolongation of the period without coma or delirium in the ICU.

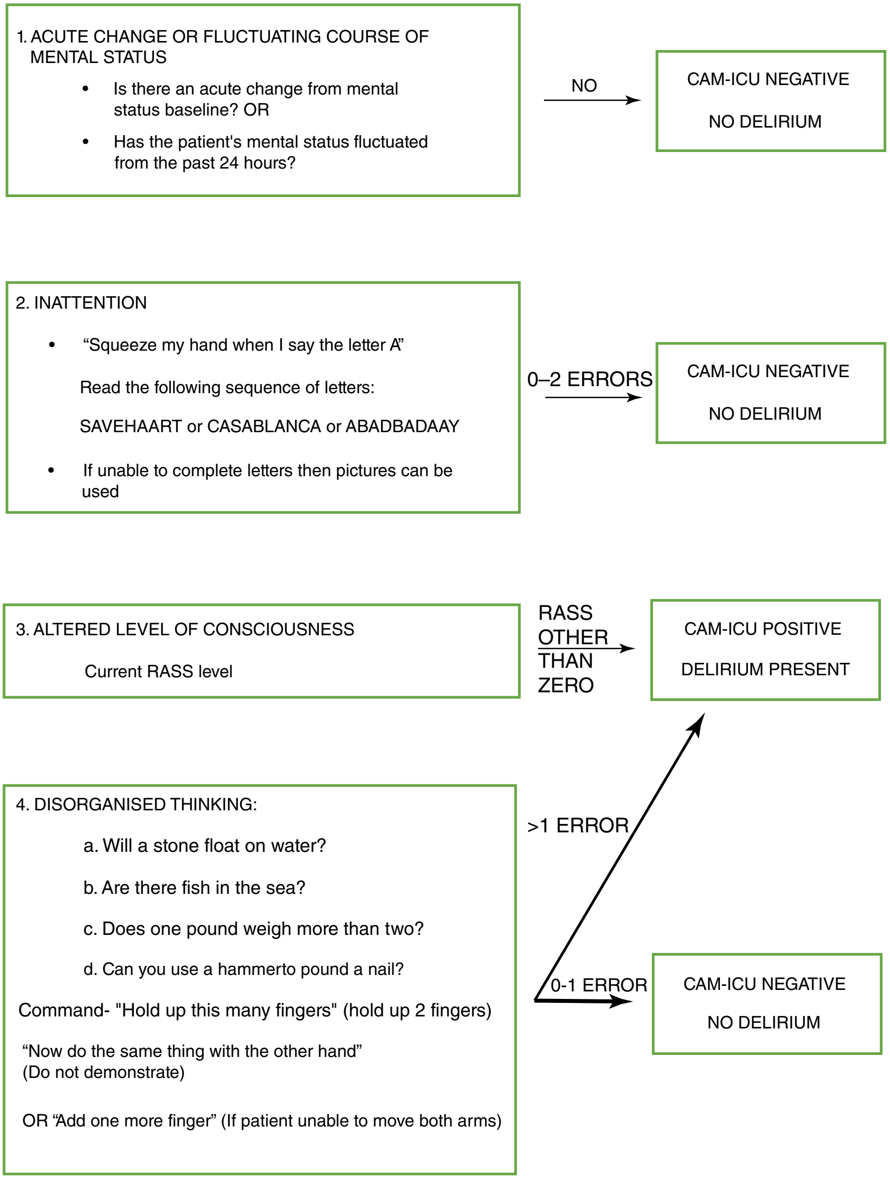
1. ACUTE CHANGE OR FLUCTUATING COURSE OF MENTAL STATUS
• Is there an acute change from mental status baseline? OR
• Has the patient's mental status fluctuated from the past 24 hours?
NO
CAM-ICU NEGATIVE
NO DELIRIUM
2. INATTENTION
• "Squeeze my hand when I say the letter A"
Read the following sequence of letters:
SAVEHAART or CASABLANCA or ABADBADAAY
• If unable to complete letters then pictures can be used
0–2 ERRORS
CAM-ICU NEGATIVE
NO DELIRIUM
3. ALTERED LEVEL OF CONSCIOUSNESS
Current RASS level
RASS OTHER THAN ZERO
CAM-ICU POSITIVE
DELIRIUM PRESENT
4. DISORGANISED THINKING:
a. Will a stone float on water?
b. Are there fish in the sea?
c. Does one pound weigh more than two?
d. Can you use a hammerto pound a nail?
Command- "Hold up this many fingers" (hold up 2 fingers)
"Now do the same thing with the other hand"
(Do not demonstrate)
OR "Add one more finger" (If patient unable to move both arms)
>1 ERROR
0-1 ERROR
CAM-ICU NEGATIVE
NO DELIRIUM

Fig. 26.3 The confusion assessment method for the ICU (CAM-ICU) flowsheet

- **A**ssess, prevent, and manage pain
- **B**oth Spontaneous Awakening Trials (SATs) and Spontaneous Breathing Trials (SBTs)
- Attention to the **C**hoice of analgesia and sedation
- **D**elirium monitoring and management

Table 26.9 Intensive care delirium screening checklist (ICDSC)

1	ALTERED LEVEL OF CONSCIOUSNESS: coma (no response) or stupor (no response to loud voice and pain)	
	No response:	No score
	Response only to intense and repeated stimulation	No score
	Response to mild or moderate stimulation	1 point
	Normal wakefulness or sleep with easy arousal	0 point
	Exaggerated response to normal stimulation	1 point
2	INATTENTION: Difficulty following conversation or instructions, easy distractions	1 point
3	DISORIENTATION: Any obvious mistake in time, place, or person	1 point
4	HALLUCINATION, DELUSION OR PSYCHOSIS	1 point
5	HYPERACTIVITY REQUIRING SEDATION OR RESTRAINTS *OR* CLINICALLY IMPORTANT PSYCHOMOTOR SLOWING	1 point
6	INAPPROPRIATE SPEECH OR MOOD	1 point
7	DISTURBANCE IN SLEEP OR WAKE CYCLE: frequent spontaneous awakening, sleeping less than 4 hours/night	1 point
8	FLUCTUATION IN SYMPTOMS	1 point

A score of ≥4 is positive for delirium (with scores of 1 to 3 termed “subsyndromal delirium”)

  - **E**arly mobility and exercise
  - **F**amily engagement and empowerment
- Role of physical restraints: Medical staff can consider using physical restraints to improve patient safety, protect staff from combative patients, prevent self-removal of medical devices, regulate patient behavior, and maintain patient posture/position. In a few studies, the use of physical restraints was associated with a prolonged ICU stay, increased agitation, increased demand for opioids and sedatives, and risk of delirium or disorientation.
- Manage sleep disturbances in the ICU:
  - Sleep disturbance in the ICU could be in any of the phases—sleep segmentation, increased light sleep (N1 + N2 stage), and decreased rapid eye movement (REM) sleep.
  - Potential causes of sleep disturbance include the following:
    - Environment of the ICU
    - Continuous bright lights and alarms
    - Treatment process, pain, and ventilation
    - Disease-related events like systemic inflammatory conditions, drugs, and the mode of the ventilator
  - The negative adverse effects of sleep disturbances include delirium, longer duration of mechanical ventilation, and decreased immune function. According to the 2018 PADIS guidelines, using the assist-control mode at night may help improve sleep quality in comparison to using the pressure-support mode.

- A sleep-promoting protocol should be used to improve the sleep of critically ill patients. This includes nonpharmaceutical strategies and pharmacologic treatment includes sleep-inducing drugs (melatonin, dexmedetomidine, and propofol).
- Immobility (Rehabilitation/Mobilization):
  - Rehabilitation in critically ill patients is related to a shortened duration of delirium, mechanical ventilation, and ICU stay. Though, no evidence of improvement in mortality, several RCTs have reported that intensive care rehabilitation can strengthen limb and respiratory muscle strength, improve physical function and quality of life, shorten the duration of delirium and mechanical ventilation, and shorten the ICU length of stay.

Suggested Reading

Barnes-Daly MA, Phillips G, Ely EW. Improving hospital survival and reducing brain dysfunction at seven California community hospitals: Implementing PAD guidelines via the ABCDEF bundle in 6,064 patients. Crit Care Med. 2017;45:171–8. *Higher ABCDEF bundle compliance was independently associated with improved survival and more days free of delirium and coma after adjusting for age, severity of illness, and presence of mechanical ventilation*

Devlin JW, Skrobik Y, Gélinas C, Needham DM, et al. Clinical practice guidelines for the prevention and management of pain, agitation/sedation, delirium, immobility, and sleep disruption in adult patients in the ICU. Crit Care Med. 2018;46(9):e825–73. *Recent guidelines for the prevention and management of pain, agitation/sedation, delirium, immobility, and sleep disruption in adult patients*

Morandi A, Brummel NE, Ely EW. Sedation, delirium and mechanical ventilation: the 'ABCDE' approach. Curr Opin Crit Care. 2011;17:43–9. *Outcomes of critically ill patients can be improved by applying evidence-based therapies for the "liberation" from mechanical ventilation such as the "ABCDE" bundle to improve the management of such patients*

Morandi A, Piva S, Ely EW, Myatra SN, Salluh JIF, Amare D, Azoulay E, Bellelli G, Csomos A, Fan E, Fagoni N, Girard TD, Heras La Calle G, Inoue S, Lim CM, Kaps R, Kotfis K, Koh Y, Misango D, Pandharipande PP, Permpikul C, Cheng Tan C, Wang DX, Sharshar T, Shehabi Y, Skrobik Y, Singh JM, Slooter A, Smith M, Tsuruta R, Latronico N. Worldwide survey of the "assessing pain, both spontaneous awakening and breathing trials, choice of drugs, delirium monitoring/management, early exercise/mobility, and family empowerment" (ABCDEF) bundle. Crit Care Med. 2017;45(11):e1111–22.

Murray MJ, DeBlock H, Erstad B, et al. Clinical practice guidelines for sustained neuromuscular blockade in the adult critically ill patient. Crit Care Med. 2016;44:2079.

Website

www.icudelirium.org. *A website of Vanderbilt University for update and practice parameters on ICU delirium*

Quality Control

27

Subhash Todi and Ashit Bhagwati

Case 1
A 70-year-old male patient with dementia and Parkinson's disease was admitted to the ICU in the confusional state. He fell from his bed on the night of admission and suffered scalp injuries. How would you ensure that similar accidents do not happen in the future?

Case 2
A 60-year-old male patient was admitted to the hospital with hypertensive intracerebral bleed and required ventilatory support. On the fourth day of admission, he developed features of ventilator-associated pneumonia. What measures should have been in place to avoid this complication?

Case 3
A 30-year-old male patient was admitted to hospital with gastroenteritis and severe hypokalemia. He was inadvertently administered a high concentration of potassium in intravenous infusion through the central line and suffered a cardiac arrest. How could you have prevented such errors?

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In a landmark publication, *To Err Is Human: Building a Safer Health System*, a decade ago by the Institute of Medicine USA, it was described that human error was one of the common causes of morbidity, mortality, and increased healthcare costs in hospitalized patients worldwide. Experts estimate that as many as 98,000 people die every year due to medical errors in hospitals. This number is more than the number of deaths due to motor vehicle accidents, breast cancer, and AIDS—three causes that receive far more public attention. This error is even more evident in the critically ill patients in the ICU. Increasing accountability and demand from public and accrediting agencies have led to a movement quality care in ICUs.

Step 1: Understand the Concept of Quality and Safety

- Quality and safety are two sides of the same coin. Quality reflects measures that should have been taken but were not carried out (errors of omission), while safety reflects actions that were taken inappropriately (errors of commission).
- Case 1 may be taken as a quality issue as proper precautions were not taken, which led to a compromise in patient safety.
- Case 2 reflects the need for preventive protocols for ventilator-associated pneumonia to be in place, another quality control issue.
- Case 3 reflects not only an error of commission, clearly a safety issue, but also a lack of protocol for intravenous potassium infusion, a quality issue.

Step 2: Understand Donabedian's Theory on Quality Control

- Three important components are as follows:
  1. Structure (what we have)
  2. Process (what we do)
  3. Outcome (what we get)
- Structural issues consist of organizational elements, personnel, and finance and are predominantly under administrative control.
- Process issues are the care given to the patient by healthcare providers. Daily checklists of such issues are always helpful.
- Outcome reflects what happens to the patient from a morbidity and mortality point of view, given the structure in place and processes being implemented (Table 27.1).

Table 27.1 Donabedian's model of quality control

Structure	Process	Outcome
Closed model of ICU care	Compliance with hand hygiene	Crude ICU mortality
Critical care consultant availability	Family conference	Risk-adjusted ICU mortality
24 × 7 intensivist coverage	End-of-life support policies	Standardized mortality ratio = crude mortality/predicted mortality
Ward design	Compliance with ventilator bundle	Hospital mortality
Nurse–patient ratio	Compliance with central line insertion bundle	ICU length of stay
Doctor–patient ratio	Antibiotic consumption	Hospital length of stay
Policies and protocols	Implementation of catheter-related bloodstream infection prevention policies	Family satisfaction
Infectious disease consultant	Implementation of urinary tract infection prevention policies	Cost of care
Infection control nurse		Resource utilization
Multidisciplinary ward round		
Infection control committee		
Daily goal sheet		
Antibiotic form		
Adequate equipment		

Step 3: Implement Standardized Data Collecting and Reporting System

- This should be done for all three elements: structure, process, and outcome.
- It should follow the SMART principle (specific, measurable, achievable, reliable, and time-bound). A well-trained data collector is the backbone of any quality control program (Fig. 27.1).

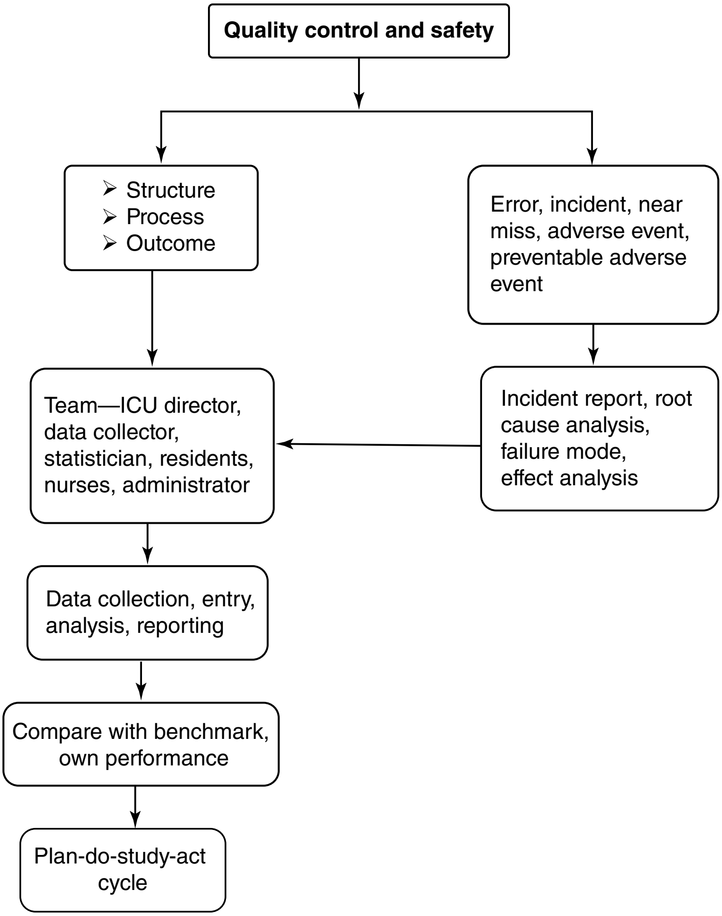
Quality control and safety
➢ Structure
➢ Process
➢ Outcome
Error, incident, near miss, adverse event, preventable adverse event
Incident report, root cause analysis, failure mode, effect analysis
Team—ICU director, data collector, statistician, residents, nurses, administrator
Data collection, entry, analysis, reporting
Compare with benchmark, own performance
Plan-do-study-act cycle

Fig. 27.1 Quality control approach in the ICU

Step 4: Understand the Principles of Data Collection

- Any data should have a numerator (affected persons) and a denominator (persons at risk) (Table 27.2).

Table 27.2 Formulae for urinary tract infections, central line-associated bloodstream infections, and ventilator-associated pneumonia

$\frac{\text{Number of catheter} - \text{associated urinary tract infections}}{\text{Number of urinary catheter} - \text{days}} \times 1000$
$\frac{\text{Number of central line} - \text{associated blood stream infections}}{\text{Number of central line} - \text{days}} \times 1000$
$\frac{\text{Number of ventilator} - \text{associated pneumonias}}{\text{Number of ventilator} - \text{days}} \times 1000$

Table 27.3 Fundamental quality indicators

(a) Early administration of acetylsalicylic acid in acute coronary syndrome
(b) Early reperfusion techniques in ST-elevation myocardial infarction
(c) Semirecumbent position in patients undergoing invasive mechanical ventilation
(d) Prevention of thromboembolism
(e) Surgical intervention in traumatic brain injury with subdural and/or epidural hematoma
(f) Monitorization of intracranial pressure in severe traumatic brain injury with pathologic CT findings
(g) Pneumonia associated with mechanical ventilation
(h) Early management of severe sepsis/septic shock
(i) Early enteral nutrition
(j) Prophylaxis against gastrointestinal hemorrhage in patients undergoing invasive mechanical ventilation
(k) Appropriate sedation
(l) Pain management in unsedated patients
(m) Inappropriate transfusion of packed red blood cells
(n) Organ donors
(o) Compliance with hand-washing protocols
(p) Information on patients' families in the ICU
(q) Withholding and withdrawing life support
(r) Perceived quality survey at discharge from the ICU
(s) Presence of an intensivist in the ICU 24 h/day
(t) Adverse events register

Adapted from Spanish quality control guideline

Step 5: Prioritize

- Identify important elements for which data need to be collected. The parameters chosen for measurement should be institution specific (Table 27.3).

Step 6: Identify Team Members

- This should be done for data collection, data entry, data analysis, and data reporting.

Step 7: Identify Benchmarks

- This should be done for comparison of data.
- There are national and international benchmarks for various quality control processes and outcomes.
- In the absence of a comparative benchmark, one can follow one's own trend and performance over time.

Step 8: Adopt the Plan-Do-Study-Act Cycle for Quality Control

- After identifying specific elements for data collection, collect, analyze, and compare reliable data with benchmarks, take corrective action, and revisit the same process periodically to maintain a standard of care.

Step 9: Understand Terminology for Reporting of Safety Issues

- Patient safety data should be reported in the format including errors, incidents, near misses, adverse events, and preventable adverse events (Table 27.4).

Table 27.4 Terminology for reporting adverse events

Patient safety	Absence of the potential for, or occurrence of, healthcare-associated injury to patients
Error	It is defined as mistakes made in the process of care that result in, or have the potential to result in, harm to patients. Mistakes include the failure of a planned action to be completed as intended or the use of a wrong plan to achieve an aim. These can be the result of an action that is taken (error of commission) or an action that is not taken (error of omission)
Incident	Unexpected or unanticipated events or circumstances not consistent with the routine care of a particular patient, which could have, or did lead to, an unintended or unnecessary harm to a person, or a complaint, loss, or damage
Near miss	An occurrence of an error that did not result in harm
Adverse event	An injury resulting from a medical intervention
Preventable adverse event	The harm that could be avoided through reasonable planning or proper execution of an action

Step 10: Implement

- One of the measures for evaluating patient safety such as an incident report, root cause analysis, and failure mode effect analysis should be implemented:
  - *Incident report*: It evaluates how a single patient comes to a harm. An incident reporting system should be voluntary, anonymous, and not linked with any form of punitive measures.
  - *Root cause analysis*: This is a more focused inquiry on certain incidents deemed to be important for patient safety. A sentinel event is identified, important preventive aspects of this event are discussed by the safety team, and safeguards are implemented.
  - *Failure mode and effects analysis*: An error-prone process is identified, and a multidisciplinary team is formed to analyze prospectively the process from multiple perspectives before a sentinel event occurs.

Step 11: Initiate a Safety and Quality Culture

- This has to come from strong leadership, primarily from the ICU director, backed up by supportive management.
- This has to be backed up by the full support and motivation of ICU staff.
- An adequate budget needs to be provided by the administration.
- Computerized physician order entry systems and clinical decision support systems go a long way in ensuring safety in the ICU by reducing human error.

Suggested Reading

Bauman KA, Hyzy RC. ICU 2020: five interventions to revolutionize quality of care in the ICU. J Intensive Care Med. 2014;29(1):13–21. *Modern ICU quality improvement initiatives include ensuring evidence-based best practices, participation in multicenter ICU collaborations, employing state-of-the-art information technology, providing point-of-care diagnostic testing, and efficient organization of ICU care delivery. This article demonstrates that each of these initiatives has the potential to revolutionize the quality of future ICU care.*

Chrusch CA, Martin CM. Quality improvement in critical care: selection and development of quality indicators. Can Respir J. 2016;2016:2516765. *Six domains of ICU function were identified: safe, timely, efficient, effective, patient/family satisfaction, and staff work life. Detailed operational definitions were developed for 22 quality indicators.*

Garland A. Improving the ICU: part 1. Chest. 2005a;127:2151–64. It discusses existing problems in ICU care and the methods for defining and measuring ICU performance.

Garland A. Improving the ICU: part 2. Chest. 2005b;127:2165–79. This second part establishes a practical framework for performance improvement and examines specific strategies to improve ICU performance, including the use of information systems.

Gawande A. The checklist. The New Yorker. 2007. December 10, 2007. *A fascinating reading on medical errors.*

Kahn JM. Bringing implementation science to the intensive care unit. Curr Opin Crit Care. 2017;23(5):398–9. *A review article on implementation science as applied to ICU*

National Nosocomial Infections Surveillance System. National Nosocomial Infections Surveillance (NNIS) System Report, data summary from January 1992 through June 2004. Am J Infect Control. 2004;32(8):470–85. *Benchmark statistics on nosocomial infections from US hospitals*

Ray B, Samaddar DP, Todi SK, Ramakrishnan N, John G, Ramasubban S. Quality indicators for ICU: ISCCM guidelines for ICUs in India. Indian J Crit Care Med. 2009;13(4):173–206.

Rosenthal VD, Maki DG, Graves N. International nosocomial infection control consortium (INICC): goals and objectives, description of surveillance methods, and operational activities. Am J Infect Control. 2010;38(2):95–104. *Benchmark statistics on nosocomial infections from developing countries*

Verburg IWM, de Jonge E. The association between outcome-based quality indicators for intensive care units. PLoS One. 2018;13(6):e0198522. *Easily quantifiable, quality indicators to assess the efficiency of ICU care are based on readmission to the ICU and ICU length of stay. This study examined whether there is an association between case-mix adjusted outcome-based quality indicators in the general ICU population as well as within specific subgroups.*

Websites

http://www.isccm.org. *A very comprehensive guideline on quality control from developing country's perspective.*

http://www.semicyuc.org/calidad/quality_indicators. *An exhaustive literature from Spain on quality control guideline.*

Acute Dermatological Emergencies in the ICU

28

Aakriti Chawla

Case Vignette

A 45-year-old female, presenting with drowsiness and a heart rate of 125 beats per minute, reported sloughing of the skin for the past two days. She had been on a new medication, phenytoin, for her history of seizures for five days before developing fluid-filled lesions and darkened skin that subsequently sloughed off, involving approximately 70% of her body surface area.

She complains of fever, eye discharge, nasal crusting, and raw wounds in the mouth and genitalia with adherent black, necrotic crusting. She has been unable to eat or drink for two days, leading to weakness, drowsiness, severe dehydration, and low urine output.

Acute dermatological emergencies are skin conditions with life-threatening implications and require utmost care and attention with intensive management in the ICU.

The most common ones are due to drug reactions or infections manifesting as Steven–Johnson syndrome-toxic epidermal Necrolysis (SJS-TEN), DRESS (drug rash eosinophilia and systemic symptoms), staphylococcal scalded skin syndrome (SSSS), acute generalized exanthematous pustulosis (AGEP), meningococcaemia, necrotizing fasciitis, purpura fulminans, and severe cutaneous vasculitis.

Prompt recognition and management are crucial to prevent morbidity, mortality, and long-term sequelae. This chapter will provide an overview of how to approach and manage some such patients in the ICU setting and highlight the importance of multidisciplinary collaboration.

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Step 1: Initiate Cardiopulmonary and Fluid Resuscitation

- Assess the patient's vitals and general condition: Patients presenting with drug reactions may arrive in an altered sensorium. Ensure that vitals are stable, and promptly secure an intravenous (IV) line for fluid resuscitation, which is critical in managing patients with Stevens–Johnson syndrome-toxic epidermal necrolysis (SJS-TEN). Admit the patient to the special unit or intensive care unit.
- Importance of fluid resuscitation and temperature management: These are paramount because denuded skin leads to significant water loss, and mucosal involvement reduces oral intake, exacerbating dehydration. Fluid requirements in SJS-TEN are approximately two-thirds of what is required for burn patients.
- Fluid management guidelines: In the first 24 h, administer 2 mL/kg per percentage of body surface area affected. Subsequently, fluids should be adjusted based on strict input–output monitoring to maintain a urine output of 0.5–1 mL/kg/h.

Step 2: Clinical Assessment

1. *Take a Detailed History*

   A thorough history is critical in patients suspected of having Stevens–Johnson syndrome-toxic epidermal necrolysis (SJS-TEN). This should include the following:
   - Timeline of symptoms: Document the onset and progression of lesions, typically beginning with bullae or vesicles that progress to sloughing of dark, necrotic skin.
   - Extent of skin and mucosal involvement: Assess symptoms such as oral, genital, and ocular mucositis, which are hallmark features of SJS-TEN.
   - Medication history: Identify any recently started medications, as causative drugs are often introduced 5–30 days before symptom onset. Include over-the-counter drugs, herbal supplements, and new treatments initiated for other conditions.
   - Focus on temporal correlations between the introduction of the medication and symptom onset.
2. *Rule Out the Culprit Drug*
   - Stop the offending drug: Discontinuation of the causative agent is the most critical step in management. This includes medications with a high risk of SJS-TEN (see Table 28.1).
   - Consider cross-reactivity: Be vigilant about drugs within the same pharmacological group that may pose similar risks. Avoid reintroducing these medications unless necessary and under strict monitoring.
3. *Perform a Detailed Physical Examination*
   - Lesion characterization: Document the appearance, distribution, and extent of lesions. Most cases involve painful, fluid-filled vesicles or bullae with subsequent sloughing of necrotic epidermis (Figs. 28.1, 28.2, 28.3, 28.4, and 28.5).

Table 28.1 Drugs causing Steven–Johnson syndrome-toxic epidermolysis

Drugs with a high risk of inducing SJS-TEN	Drugs with moderate (significant but substantially lower) risk for SJS-TEN	Drugs with lower risk/ suspected association
Allopurinol Lamotrigine Cotrimoxazole (anti-infective sulphonamides and sulfasalazine) Nevirapine NSAIDS (oxicam type, e.g., meloxicam, etoricoxib) Phenobarbital Phenytoin Carbamazepine	Cephalosporins Macrolides Quinolones Tetracyclines NSAIDS (acetic acid type, e.g., diclofenac) Oxcarbazepine Rifampin Amifostine	Pantoprazole Glucocorticoids Omeprazole Tetrazepam Levetiracetam Terbinafine Dipyrone (metamizole)

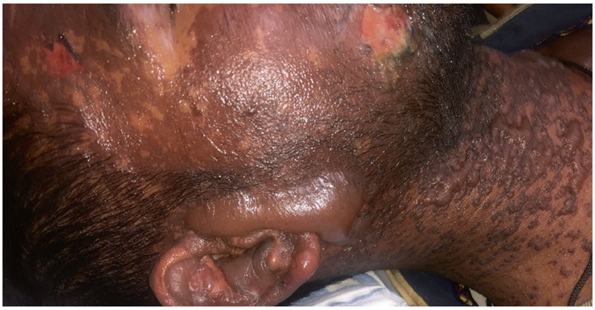

Fig. 28.1 Dead, necrotic skin with bullae and few erosions

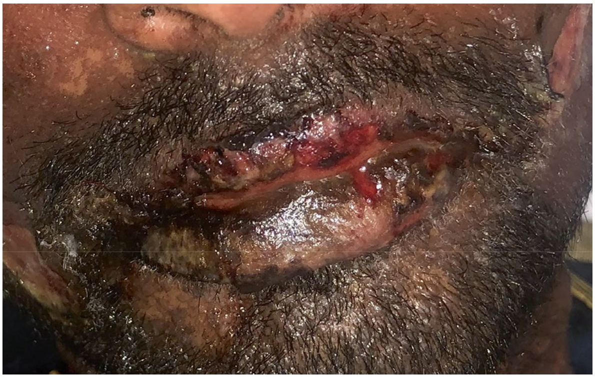

Fig. 28.2 Lips showing adherent necrotic crust

- Body surface area (BSA) involvement: Assess the extent of skin detachment using the "Rule of Nines" commonly applied for burn patients. Categorize the condition based on BSA involvement as:
  - *SJS*: BSA <10%
  - *SJS-TEN overlaps*: BSA 10–30%
  - *TEN*: BSA >30%

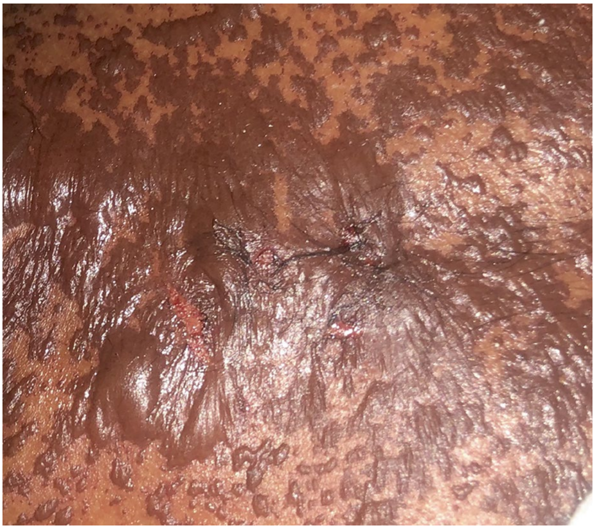

Fig. 28.3 Showing bullae and dark necrotic skin which has separated

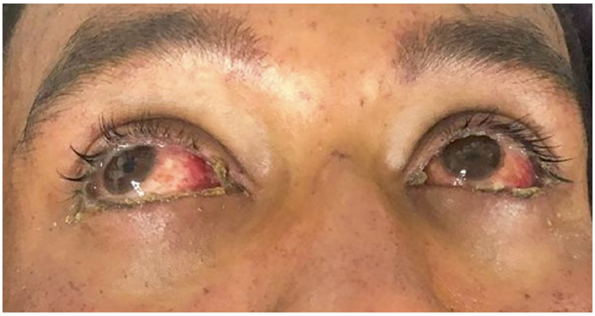

Fig. 28.4 Showing conjunctivitis in the eyes and sticky yellow discharge

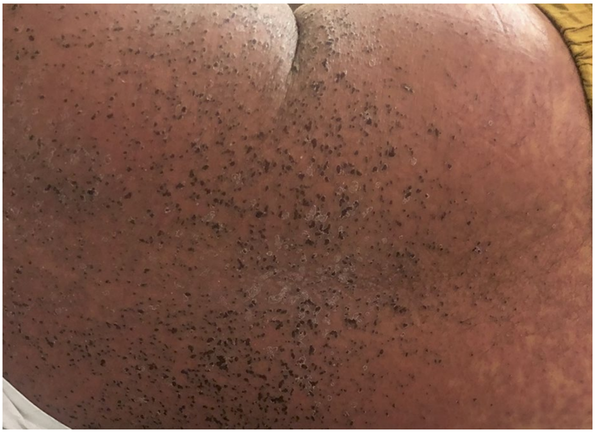

Fig. 28.5 Showing coalescing erythematous papules with dead necrotic skin adherent

  - Mucosal involvement: Examine the mouth, eyes, genitalia, and other mucosal sites for erosions, crusting, and necrotic sloughing.

Step 3: Multidisciplinary Approach

- *Dermatology consultation*: Obtain an expert dermatology opinion to confirm the diagnosis and guide management, especially for drug rashes requiring complex care.
- *Involve other specialists*: Include ophthalmology, gynecology, or urology for managing mucosal complications and critical care for severely ill patients.
- *Analyze ongoing medication needs*.
  - *Risk–benefit analysis*: For patients on multiple medications, evaluate which drugs are essential and safe to continue. Consider withholding non-essential medications until they can be definitively cleared as non-contributory.
  - *Document allergies*: Record suspected and confirmed drug allergies to prevent future exposures.
- *Systemic involvement*: Monitor for signs of multisystem complications, such as sepsis, acute kidney injury, or respiratory distress, which are common in SJS-TEN.

Step 4: Check Vitals, Perform Arterial Blood Gas Analysis

The next step in managing patients with drug-induced rashes, such as SJS-TEN, is to assess the mortality risk. This involves:

- *Monitoring vital signs*: Continuously check for abnormalities such as hypotension, tachycardia, fever, or hypoxia, which may indicate sepsis or impending organ failure.
- *Arterial blood gas (ABG) analysis*: Perform ABG to evaluate oxygenation and acid–base status, and identify any respiratory compromise or metabolic disturbances.
- A simple tool such as SCORETEN (Table 28.2) helps determine the prognosis in SJS-TEN patients. This scoring system incorporates parameters like age, heart rate, presence of malignancy, extent of epidermal detachment, and others, to predict mortality risk.
- Patients with SJS-TEN are at high risk of sepsis, which is a leading cause of mortality.
- Other major contributors to poor outcomes include respiratory distress and multi-organ failure.
- Early identification of these risks and prompt management in a critical care setting are essential to improve survival outcomes.

Round-the-clock monitoring of temperature and vitals along with fluid input–output is required.

Table 28.2 SCORETEN: A prognostic scoring system for patients with epidermal necrolysis

Prognostic factors	Points
Age ≥40 years	1
Associated cancer	1
Heart rate (beats/minute) ≥120	1
Serum blood urea nitrogen >28 mg/dL (10 mmol/L)	1
Detached or compromised body surface ≥10%	1
Serum bicarbonate <20 mEq/L (<20 mmol/L)	1
Serum glucose >250 mg/dL (>14 mmol/L)	1
More risk factors indicate a higher score and a higher mortality rate (%) as follows:	MORTALITY RATE (%)
0–1	3.2% (CI: 0.1–16.7)
2	12.1% (CI: 5.4–22.5)
3	35.3% (CI: 19.8–53.5)
4	58.3% (CI: 36.6–77.9)
≥5	>90% (CI: 55.5–99.8)

Step 5: Perform Investigations

1. *Comprehensive Laboratory Workup*
   - *Complete blood count (CBC)*: Assess for leukocytosis or leukopenia, which may indicate infection or immune dysregulation.
   - *Liver and kidney function tests (LFTs and KFTs):* Evaluate for organ involvement or drug-induced toxicity.
   - *Blood glucose*: Monitor for hyperglycemia, which can indicate stress or infection.
   - *C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR)*: Measure inflammatory markers.
   - *Coagulation profile*: Check for coagulation abnormalities, as these are common in severe systemic illnesses.
   - *Complement levels*: Evaluate for immune system activation or deficiency.
   - *Urinalysis*: Identify renal complications or secondary infections.
2. *Microbiological Investigations*
   - *Cultures*: Obtain bacterial and fungal cultures from wounds, blood, and urine to identify potential infection sources and prevent sepsis.
   - *Mycoplasma pneumoniae testing*: Some studies suggest an association between *Mycoplasma pneumoniae* and toxic epidermal necrolysis (TEN). Polymerase chain reaction (PCR) or serology for this pathogen may be indicated.
3. *Imaging Studies*
   - *Chest radiograph*: Perform in all patients to detect pulmonary involvement, such as pneumonia or interstitial pneumonitis.
4. *Specific Diagnostic Tools*
   - *Indirect immunofluorescence on skin biopsy*: This test may help confirm the diagnosis of SJS-TEN, particularly in ambiguous cases.
   - *Nikolsky's sign*: A simple bedside test where lateral pressure applied to a bulla causes epidermal shearing, indicating epidermal necrolysis. Although not

specific for SJS-TEN, it is a useful clinical indicator of the severity of skin involvement.

Timely and comprehensive investigations are critical for confirming the diagnosis, identifying complications, and guiding treatment in SJS-TEN patients.

Step 6: Initiate Specific Treatment

Comprehensive management of Stevens–Johnson syndrome-toxic epidermal necrolysis (SJS-TEN) requires addressing systemic involvement in addition to supportive care, wound care, and systemic therapy.

- *Supportive Care*
- Supportive measures remain the cornerstone of SJS-TEN management, focusing on fluid resuscitation, electrolyte balance, nutritional support, complications prevention, and organ function monitoring and support (Table 28.3).

Table 28.3 Supportive care of SJS-TEN

Mucosa involved	Symptoms	Treatment	Possible long-term sequelae
Eyes	Corneal and conjunctival epithelial defects Conjunctivitis Chemosis Psuedomembrane formation Adhesions/synechiae	Saline rinses Lubricants Topical corticosteroids/antibiotics Daily examination by an ophthalmologist with the sweeping of the eye	Fibrosis Corneal ulcerations Entropion symblepharon Trichiasis Alterations in vision Chronic inflammation
Oral cavity	Painful mucosal erythema Bullae and consequently erosions may spread to the larynx and pharynx Adherent necrotic crusting on lips	If no infection topical corticosteroid may be considered Mucoprotectant and antiseptic mouthwash Benzydamine hydrochloride anti-inflammatory mouth wash Emollients on lips	Dysgeusia Dryness Late alterations of teeth
Urogenital	Dysuria Urinary retention Erosions of external genitalia	Catheterization Frequent use of emollients Mild corticosteroid cream with antimicrobial activity Silicone sheet dressings in vulva/vagina	Preventing urethral strictures Preventing stricture formation Dyspareunia

- *Wound Care*
  - Deroofing of large bullae to allow separated epidermis to act as a biological dressing.
  - Gentle cleansing is performed with sterile water or chlorhexidine.
  - Dressings with petroleum- or paraffin-impregnated gauze, cleaned with normal saline during dressing changes.
  - Use air-fluidized mattresses to minimize shearing forces and pressure injuries.
- *Nutritional Support and Analgesia*
  - Ensure adequate nutritional support, with 20–25 kcal/kg per day, especially in cases of mucosal involvement, through enteral or parenteral feeding. Give 25–30 kcal/kg per day during recovery, the anabolic phase of the disease. Protein should be provided as 1.5–2 gm/kg body weight.
  - Provide analgesia using paracetamol or opioids for effective pain management.
- *Infection Monitoring and Management*
  - Vigilantly monitor for signs of infection, as sepsis is a leading cause of mortality.
  - Repeated surveillance cultures of the skin, blood, catheters, gastric, and urinary tubes should be obtained at regular intervals (e.g., every 48 h) to facilitate early infection detection.
  - Initiate empirical or culture-specific antibiotics based on clinical suspicion or confirmed infection. Prophylactic antibiotics are not recommended.

Systemic Therapy

There is no proven pharmacologic treatment for SJS/TEN. The evidence supporting these interventions is limited, and none can be definitively recommended. However, findings from several meta-analyses indicate a potential benefit of some of these.

- *Cyclosporin*: Growing evidence from case series and meta-analyses suggests that early cyclosporine use during the acute phase may reduce mortality. Some experts recommend initiating cyclosporine (3–5 mg/kg/day) as adjunctive therapy within 24–48 h of symptom onset for 10 days followed by tapering.
- *Systemic Steroids*: While controversial, still commonly used, the efficacy of systemic corticosteroids has not been proven. A 2017 meta-analysis of 1209 patients, including 367 treated with systemic corticosteroids, found a modest reduction in mortality risk compared to supportive care alone. Thus, routine use of systemic corticosteroids cannot be recommended. They should be used only on a case-to-case basis.
  - *Prednisolone*: 0.5–1 mg/kg/day for 10 days, followed by tapering.
  - *IV Methylprednisolone Pulse Therapy*: 500 mg intravenously for three consecutive days.
- *IV Immunoglobulin (IVIg)*: 0.5–1 g/kg daily for 3–4 consecutive days. Mostly recommended against using intravenous immune globulin (IVIG) as monotherapy for SJS/TEN. Meta-analyses have shown no clear survival benefit with IVIG alone. Its role in combination with systemic steroids requires further investigation.

Organ-Specific Involvement and Management

- *Gastrointestinal Involvement*
  - Symptoms: Includes malabsorption, melena, and, rarely, perforation.
  - Management: Ensure nutritional support and monitor for gastrointestinal bleeding or perforation.
- *Renal Involvement*
  - Presentation: Hematuria, proteinuria, microalbuminuria, azotemia, and acute kidney injury (AKI) due to tubule damage or end-organ hypoperfusion.
  - Management: Monitor renal function and manage AKI with fluid resuscitation or renal replacement therapy if indicated.
- *Pulmonary Involvement (40%)*
  - *Symptoms*: Detachment of the epithelial lining causing dyspnea, bronchial hypersecretion, increased respiratory rate, and progression to pulmonary edema, pneumonia, atelectasis, or acute respiratory failure.
  - *Risk Factors for Mechanical Ventilation*:
    - Hemoglobin <8 g/dL
    - BSA involvement >10%
    - WBC >12,000/mm^3
    - Serum bicarbonate <20 mmol/L
    - Serum urea >10 mmol/L
    - Bacteremia, shock, or organ failure at admission.
  - *Bronchoscopy*: This may be required to confirm bronchial involvement. Mechanical removal of sloughed bronchial epithelium can prevent airway obstruction and atelectasis.
  - *Ventilation*:
    - Noninvasive ventilation is contraindicated due to skin and mucosal involvement.
    - Oral intubation is challenging due to mucosal lesions, requiring skilled airway management.
      - Eye care is done to prevent long-term complications. In severe cases, use preservative-free corticosteroid eye drops, and cover the eye with cryopreserved amniotic membrane.

Additional Supportive Measures

- *Prevention of complications:*
  - *Stress ulcers*: Use proton pump inhibitors (PPIs) or H2 blockers.
  - *Deep vein thrombosis (DVT)*: Employ anticoagulants if no contraindications exist.
  - *Disseminated intravascular coagulation (DIC)*: Address promptly in patients with sepsis.
  - *Hyperglycemia/Hypoglycemia*: Manage per intensive care protocols.
- *Close Monitoring*: Monitor all parameters for 7–10 days, the critical period for complications and mortality.

To improve outcomes in SJS-TEN patients, a multidisciplinary approach involving dermatology, critical care, pulmonology, nephrology, and gastroenterology is essential.

Case Vignette 2

A 65-year-old male, with a known case of diabetes and hypertension, presented to the emergency department as a referral from another hospital. He had been admitted to the previous hospital for the treatment of a stroke for the past four weeks. During this time, he received antibiotics and various other medications. He now complains of reddish, scaly lesions all over his body for the past five days. His eosinophil count, transaminase levels, and urea/creatinine levels are elevated to three times the upper limit of normal. He is drowsy, has low urine output, and is tachycardic.

Drug reaction with eosinophilia and systemic symptoms (DRESS) is a rare but potentially life-threatening hypersensitivity reaction triggered by certain drugs. It is marked by a skin eruption, hematologic abnormalities, lymphadenopathy, and/or internal organ involvement. Other features include eosinophilia, as well as typical and atypical lymphocytosis. A distinguishing characteristic of DRESS is the prolonged latency period between drug administration and the onset of symptoms, which usually ranges from 2 to 8 weeks Most cases are linked to antiseizure medications, allopurinol, antibacterial sulfonamides, minocycline, and vancomycin. The causative drugs are listed in Table 28.4.

Table 28.4 Drugs implicated in DRESS

High-risk drugs	Low-risk drugs
Allopurinol	Beta lactams
Aromatic and anti-epileptic agents	Amoxicillin
Carbamazepine	Ampicillin
Phenytoin	Piperacillin
Lamotrigine	Others
Oxcarbazepine	NSAIDs (celecoxib, ibuprofen, diclofenac)
Phenobarbital	Olanzapine
Sulphonamides	Fluoxetine
Sulfasalazine	Imatinib
Dapsone	Sorafenib
Cotrimoxazole	Vemurafenib
Sulfadiazine	Omeprazole
Vancomycin	Raltegravir
Minocycline	
Nevirapine	
Antituberculosis agents	
Rifampicin	
Isoniazid	
Ethambutol	
Pyrazinamide	

Some studies also suggest an association between DRESS and the reactivation of viruses from the *Herpesviridae* family, with HHV-6 being the most commonly implicated virus.

Step 1: Initiate Resuscitation

- Assess the vitals and general condition of the patient and resuscitate as mentioned in Chap. 24.

Step 2: Take a Clinical History and Perform an Examination

- Patients typically present with a polymorphic eruption, which may include maculopapular rashes, purpura, infiltrated plaques, exfoliation, target-like lesions, or pustules.
- More than 50% of the body surface area (BSA) is usually involved. Pruritus and facial swelling are common features in most cases.
- Mucosal involvement may also occur but is generally less severe compared to Stevens–Johnson syndrome (SJS) or toxic epidermal necrolysis (TEN).

Step 3: Make a Diagnosis

The diagnosis of DRESS can be confirmed or excluded using the criteria outlined in the RegiSCAR scoring system (Table 28.5).

Table 28.5 RegiSCAR scoring system for diagnosis of DRESS

Clinical parameters	Score			comments
	−1	0	1	
Fever ≥101.3 °F or 38.5 °C	No/ unknown	Yes		
Lymphadenopathy		No/ unknown	Yes	>1 cm, at least 2 sites
Hematological abnormalities				
Eosinophilia $\geq 0.7 \times 10^9$ or ≥10% if leukopenia		No/ unknown	Yes	Score 2 points if $\geq 1.5 \times 10^9$
Atypical lymphocytes		No/ unknown	Yes	
Skin rash				
Rash suggestive of DRESS	No	unknown	Yes	Suggestive features ≥2 symptoms- facial edema infiltration desquamation purpura
Extent ≥50% BSA		No/ unknown	Yes	

(continued)

Table 28.5 (continued)

	Score			
Clinical parameters	−1	0	1	comments
Skin biopsy suggestive of DRESS	No	Yes/ unknown		
Organ involvement		No	Yes	1 point for each organ involvement, maximum score: 2
Disease duration ≥15 days	No/ unknown	Yes		
Exclusion of other causes		No/ unknown	Yes	1 point if 3 of the following tests are performed and are negative: hepatitis A, HBV, HCV, mycoplasma, chlamydia, ANA, blood culture

Total score
<2: excluded
2–3: possible
4–5: probable
≥6: definite

- It is essential to differentiate DRESS from other conditions, including:
  - Other adverse drug reactions.
  - Hypereosinophilic syndromes.
  - Acute systemic lupus erythematosus (SLE).
  - Viral exanthems.
  - Lymphoma.

Step 4: Send Investigations

Initial Laboratory Investigations for Confirming the Diagnosis

1. *Basic Evaluations*:
   - Complete blood counts (CBC) with differential leukocyte count.
   - Peripheral blood smear to detect atypical lymphocytes.
   - Inflammatory markers.
   - Blood PCR for viral reactivation: *HHV-6*, *HHV-7*, CMV, and EBV.
2. *Assessment of Organ Involvement:*
   - *Liver Function Tests:*
     - SGPT/ALT ≥2 times the upper limit of normal (ULN).
     - Alkaline phosphatase ≥1.5 times ULN on at least two occasions.
   - *Kidney Function Tests:*
     - Serum creatinine ≥1.5 times the baseline value on at least two occasions.
     - Proteinuria >1 g/day, hematuria, or decreased creatinine clearance.
   - *Cardiac Evaluation:*
     - Troponin levels.
     - Creatine kinase.
     - ECG to assess cardiac involvement.

- *Pancreatic Evaluation:*
  - Serum amylase and lipase levels ≥2 times ULN.
- *Additional Investigations:*
  - Coagulation profile.
  - Imaging: CT scan, ultrasound, etc.
  - Skin biopsy (if required for diagnostic clarification).
- For the exclusion of alternate diagnoses, blood cultures, ANA, anti-nuclear antibodies serology for viral hepatitis, and lymph node biopsy may be done.

Step 5: Evaluate Organ Involvement

Approximately 35% of patients with DRESS have involvement of two or more internal organs.

1. *Liver Involvement:*
   - Liver injury is the most common visceral manifestation of DRESS, presenting with cholestatic, hepatocellular, or mixed patterns.
   - Elevation of liver enzymes to more than three times the upper limit of normal is commonly observed.
   - Some patients may develop acute liver failure requiring liver transplantation.
2. *Kidney Involvement:*
   - Kidney manifestations range from proteinuria to kidney failure or acute interstitial nephritis.
   - Risk factors include older age and pre-existing kidney or cardiovascular disease.
   - Kidney involvement is commonly associated with allopurinol use.
3. *Pulmonary Involvement:*
   - Typically presents with symptoms like shortness of breath and dry cough.
   - Severe cases can present as acute interstitial pneumonitis, pneumonia, ARDS, or pleuritis.
   - Chest X-rays and CT scans can help visualize infiltrates and/or effusions.
4. *Cardiac Involvement:*
   - Cardiac involvement is a poor prognostic factor, presenting with hypertension, chest pain, dyspnea, tachycardia, and ECG changes.
   - There are two primary types:
     - *Hypersensitivity myocarditis*, associated with non-specific symptoms.
     - *Acute necrotizing eosinophilic myocarditis*, a severe form with high mortality.
   - Diagnosis can be confirmed through endomyocardial biopsy.
5. *Other System Involvement:*
   - *Nervous System*: Bell’s palsy, vasculitis, meningitis, and encephalitis.
   - *Gastrointestinal System*: Pancreatitis, colitis, gastrointestinal bleeding, perforation, and cholecystitis.

- *Other Rare Manifestations*: Thyroid dysfunction, hemophagocytic syndrome, and uveitis.

The clinical course of DRESS is variable, and there are no reliable markers to predict outcomes. Reactivation of *Cytomegalovirus* (CMV) has been associated with poor prognosis.

Step 6: Specific Treatment

Management of DRESS depends on the severity of organ involvement.

1. *General Principles:*
   - The first and most crucial step is the immediate withdrawal of the suspected drug.
   - Supportive care includes fluid resuscitation, nutritional support, proper skin care, and avoiding the introduction of any new medications.
   - Management typically requires a multidisciplinary approach, with consultations from specialists as needed.
2. *Treatment Based on Severity:*
   - *Mild Cases*:
     - Outpatient treatment with corticosteroids usually suffices.
   - *Moderate Cases:*
     - Super-high potency topical steroids combined with systemic steroids tapered over three months or longer are recommended.
   - *Severe Cases:*
     - Patients with extensive rash and severe systemic symptoms should be hospitalized for assessment and treatment.
     - Systemic corticosteroids are the mainstay.
     - Oral prednisone (0.5–1 mg/kg/day) is given until clinical and laboratory improvement is noted, followed by tapering over 8–12 weeks or longer to prevent relapse.
     - Alternatively, pulse-dose intravenous methylprednisolone (250–500 mg/day for 2–4 days) may be used, followed by oral prednisone (1 mg/kg/day) tapered over 8–12 weeks. However, this approach may increase the risk of *Cytomegalovirus* (CMV) reactivation.
3. *Alternative Therapies:*
   - *Cyclosporine*:
     - For corticosteroid-refractory DRESS, oral cyclosporine (3–5 mg/kg/day, tapered over 7–14 days) is a second-line option, showing faster symptom resolution and shorter hospital stays in limited studies.
     - Not recommended for patients with kidney involvement or pre-existing chronic kidney disease.

- *JAK-STAT Inhibitors*:
  - Dosage: 10 mg/day.
  - These have shown promise in refractory cases.
- *IVIG* has limited evidence for use in DRESS.

4. *Resolution Timeline:*
   - Withdrawal of the causative drug usually results in resolution of skin and organ involvement within 15 days to 7 weeks.
   - Prolonged healing may occur in cases with viral reactivation, atypical lymphocytosis, or severe liver dysfunction.
   - Flare-ups may occur if steroid treatment is stopped prematurely or if HHV-6 reactivation occurs.

Resolution and Prognosis

Withdrawal of the causative drug typically leads to the resolution of skin and organ involvement, which can take anywhere from 15 days to 7 weeks or months.

Factors associated with prolonged healing include:

- Viral reactivation.
- Atypical lymphocytosis.
- Severe liver dysfunction.

Flare-ups may occur if steroid treatment is discontinued prematurely or if *HHV-6* reactivation takes place.

Suggested Reading

Clark AE, Fook-Chong S, Choo K, et al. Delayed admission to a specialist referral center for Stevens-Johnson syndrome and toxic epidermal necrolysis is associated with increased mortality: a retrospective cohort study. JAAD Int. 2021;4:10.

Lee HY. Wound management strategies in Stevens-Johnson syndrome/toxic epidermal necrolysis: an unmet need. J Am Acad Dermatol. 2018;79:e87.

Phan K, Oh LJ, Issler-Fisher A, et al. Ventilatory support in Stevens-Johnson syndrome and toxic epidermal necrolysis: a systematic review and meta-analysis. J Dermatolog Treat. 2022;33:525.

Schunkert EM, Divito SJ. Updates and insights in the diagnosis and management of DRESS syndrome. Curr Dermatol Rep. 2021;10:192.

Seminario-Vidal L, Kroshinsky D, Malachowski SJ, et al. Society of Dermatology Hospitalists supportive care guidelines for the management of Stevens-Johnson syndrome/toxic epidermal necrolysis in adults. J Am Acad Dermatol. 2020;82:1553. *Recent guidelines.*

Pharmacological Principles and Drug Interactions in the ICU

29

Anuj M. Clerk and Ritesh Shah

Case Vignette

An 84-year-old male was admitted to the intensive care unit with a history of syncopal attack at home, after a day-long fast for religious reasons. In the emergency department, his heart rate was 35/min, and BP was 80/60 mmHg. His lab results were normal except for a serum creatinine level of 3.2 mg/dl (baseline: 1.4 mg/dl, 3 months ago) and a potassium level of 6.2 meq/L. ECG showed a complete heart block. On medical reconciliation, he was found to be taking atenolol 50 mg once daily and telmisartan 40 mg once daily for his hypertension. His son also showed a tablet of aceclofenac (100 mg) that he had purchased over the counter from a chemist shop for his back pain.

Intensivists should have a sound knowledge of pharmacology, as it not only helps in diagnosing the etiology of serious illness due to drug side effects but also aids in patient treatment. ICU patients often suffer from poor absorption from the gut (due to poor perfusion, dysmotility, mucosal edema, and drug-food interactions caused by nasogastric feeds), a high volume of distribution (due to hypoproteinemia, large volume resuscitation, and high extracellular fluid from edema), low cardiac output, and maldistribution of flow (as seen in hepatorenal syndrome and abdominal compartment syndrome). Additionally, multiorgan dysfunction (liver and kidney) causes reduced metabolism, as well as drug–drug interactions. Most patients in modern ICUs are elderly with multiple comorbidities, including chronic organ dysfunctions. Failure to consider alterations in pharmacokinetics (PK) and pharmacodynamics

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(PD) characteristics can lead to suboptimal dosing, resulting in adverse outcomes, increased risk of medication errors, and adverse drug reactions.

These aspects are so dynamic and complex that, despite constant surveillance by all members of the intensive care team, additional supervision by a clinical pharmacist is highly desirable. This chapter aims to provide guiding principles for intensivists to fine-tune medication use in ICUs. Let us revisit the basics of PK-PD concepts in the context of intensive care patients.

Step 1: Check Oral Bioavailability

- It means oral absorption, the amount of drug taken orally reaching to bloodstream. The lipophilic drug diffuses across membranes and small hydrophilic (water soluble) molecule gets absorbed via small aqueous channels.
- Large water-soluble molecules and protein-bound drugs need active pumps to facilitate passage.
- Hypo perfusion, reduced gut motility (acidic drug absorbed more with gastroparesis and vice versa), use of PPI-increased pH, regular NG feeds (phenytoin and thyroxin absorption reduced markedly with food), bowel transit time (diarrhea or high output fistula—poor absorption), extent of fist pass uptake by liver (depend on liver perfusion and function), etc., lead to reduced bioavailability of medications taken orally.
- Few medications are available only in enteral form and are prone to these alterations.
- Beware of enteric-coated formulae (most of the PPI) and controlled-release formulations (like metoprolol, theophyllines, and antiparkinsonian drugs) that cannot be crushed and given through a nasogastric tube.

Step 2: Consider Edema and Volume of Distribution

- Lipophilic drugs (analgesics, sedatives, antifungals) have very high Vd (almost equal to the volume of body fluid) and depend more on liver metabolism for their elimination. So, increasing intravascular or extracellular volume by fluid resuscitation will not affect their serum concentration.
- Hydrophilic drugs (beta-lactam antibiotics) have limited Vd but vary widely with protein binding, the quantum of fluid resuscitation, and edema formation (e.g., trauma and burns resuscitation). Increasing intravascular or extracellular volume by fluid resuscitation will decrease their serum concentration.
- Most critically ill patients receive large volumes of intravenous fluids during various phases of illness, resulting in high ECF volume and subtherapeutic plasma concentrations of medication during the crucial phase of illness (Resuscitation).
- Most beta-lactam and aminoglycoside antibiotics are hydrophilic drugs while linezolid, chloramphenicol, and moxifloxacin are lipophilic drugs. Edematous

patients have less absorption of drugs injected subcutaneously (e.g., insulin, G-CSF, erythropoietin, heparin, LMWH), which further varies with skin perfusion and so very unpredictable drug levels in seriously ill patients.

Step 3: Keep in Mind Plasma Protein Binding and Free Drug Concentration

- A drop in serum albumin is an acute phase reaction and its level varies inversely with the severity of illness (recovers on convalescence). Therefore, highly protein-bound drugs like digoxin and beta-lactam antibiotics (ceftriaxone, ertapenem, flucloxacillin, daptomycin) have a high free fraction during the early phase of critical illness while the same goes down during the recovery phase. The high free fraction will also lead to increased renal clearance, so the ultimate level of free drug level is unpredictable.
- Competition at protein binding sites along with the changing quantum of such binding sites leads to major changes in the concentration of free drugs in plasma and body fluids.

Now that the drug has reached its site of action, its concentration depends on its elimination kinetics, which varies widely in ICU patients.

Step 4: Examine Organ Functions Responsible for Drug Elimination

Step 4a: Liver Dysfunction

- There is no single marker to quantify liver dysfunction. The Child–Pugh score is less sensitive and specific but useful to quantify to some extent.
- Glucuronidation is less affected than the CYP450 system in mild to moderate liver dysfunction.
- Reduction in plasma proteins and their binding affect the distribution of drugs.
- Reduction in renal function is common with chronic liver disease.
- Portosystemic shunting reduces first-pass metabolism, increasing systemic drug levels in cirrhotic patients (e.g., carvedilol, propranolol, metoprolol, midazolam, labetalol). Reduced muscle mass and decreased creatine-to-creatinine conversion lead to an overestimation of GFR by the Cockcroft–Gault equation.
- Relative refractoriness to beta-blockers and diuretics and increased sensitivity to anxiolytics, sedatives, and analgesics are noted in all patients with liver dysfunction.

Recommendations for Liver Dysfunction

Use the Child–Pugh score to quantify the severity of liver dysfunction. Use the manufacturer's recommendation based on the Child–Pugh score when available. When no such guide is available, use the following:

- Drugs with a relatively high hepatic extraction ratio have increased oral bioavailability (reduce oral loading dose); for parenteral delivery, clearance depends on hepatic blood flow—reduce maintenance doses as well.
- Drugs with a low hepatic extraction and high plasma protein binding (>90%): effect may be more than plasma level, titrate to effect, reduce maintenance dose in proportion to the Child–Pugh score.
- Drugs with a low hepatic extraction ratio and low plasma protein binding (<90%): adjust the dose aimed at maintaining total plasma drug concentration.
- Excreted unchanged by the kidney: caution—creatinine clearance overestimates GFR in liver disease patients due to low skeletal muscle mass.
- Vd of hydrophilic drug increases markedly with ascites and edema, but caution is required for renal excretion while increasing doses.
- Drugs with a narrow therapeutic window—use with caution in Child–Pugh class C cirrhotic patients.
- Drugs with predominant biliary excretion to be reduced with cholestasis conditions.

Step 4b: Augmented Renal Clearance

- As high as 65% of critically ill patients in ICU with normal plasma creatinine levels have augmented renal clearance (i.e., supranormal 120–150 ml/min) during hyperdynamic states (sepsis, trauma, burns, pancreatitis). This leads to increased elimination of antibiotics in the urine leading to subtherapeutic plasma levels.

  Loading dose with the maximum allowable dose of IV antibiotics is advisable.

Step 4c: Renal Dysfunction

- ICU patients may have stable CKD, AKI on CKD, or AKI only. Creatinine rise is a delayed and poor marker for severity of renal dysfunction and any method to estimate GFR in AKI patients is far from perfect. However, GFR-based guidance for dose adjustment for most of the medications as per manufacturer's guidance needs to be followed.
- Use of various methods of dialysis (HD, SLED, CRRT) needs dose adjustment on a daily basis as per the manufacturer's guidance. One is advised to keep a table created from such a source and keep it in the ICU for ease of access.
- Adsorption on extracorporeal circuits during CRRT, ECMO, LVAD, CPB pump, etc., needs to be accounted for and the use of TDM in such circumstances is highly encouraged where available and practical.

Step 5: Re-look at the Drug Chart for Drug Interactions Daily

- Drug interactions can be pharmaceutical (chemical or physical) or pharmacological (PK or PD related). PD-related can be antagonistic, additive, or synergistic, and PK related can be absorption, distribution, metabolism, or excretion related. Interaction can be drug–food or drug-to-drug related.

Step 5a: Drug–Drug Interactions (Table 29.1)

- The majority of drug interactions occur due to the induction or inhibition of cytochrome P450 pathway or glycoprotein P. As cytochrome P450 3A4 accounts for more than 60% of medications metabolized by this group of enzymes, it needs special attention. Intensive care practitioners must have a list of tables stating CYP450 inducers and inhibitors in the ICU.

Table 29.1 Common drug–drug interactions in ICUs as found in one study: Actual type and incidence may vary in your ICU. Lexi-Interact DDI risk category in the second column

DDI (frequency in study)	Risk category	Mechanism of effect/ interaction	Recommendation
Meropenem + valproic acid (2)	D	Meropenem may decrease the serum concentration of valproic acid.	Consider alternative antibiotic agents or antiseizure. Monitor closely if combined.
Naproxen + furosemide (1)	D	Naproxen may diminish the diuretic effect of furosemide.	Monitor for the decreased therapeutic effect of furosemide.
Ciprofloxacin + theophylline (1)	D	Ciprofloxacin may increase the serum concentration of theophylline.	Monitor for toxic effects of theophylline. Theophylline dose reductions will likely be required. Avoid combination.
Multivitamins and minerals + levothyroxine (1)	D	Multivitamins and minerals may decrease the serum concentration of levothyroxine.	Separate the oral administration of iron-containing multivitamins and levothyroxine by at least 4 h.
Naproxen + aspirin (1)	D	Additive/naproxen may enhance the adverse effect of aspirin.	Monitor for increased risk of bleeding.
Aspirin + warfarin (2)	D	Aspirin may enhance the anticoagulant effect of warfarin.	Avoid combining. Monitor for increased signs and symptoms of bleeding.

(continued)

Table 29.1 (continued)

DDI (frequency in study)	Risk category	Mechanism of effect/ interaction	Recommendation
Indomethacin or Naproxen + aspirin (1)	D	Naproxen or indomethacin may enhance the adverse effect of aspirin	Monitor for increased risk of bleeding.
Diclofenac + furosemide (1)	D	Antagonistic/ diclofenac may diminish for diuretic effect of furosemide.	Monitor for decreased therapeutic effect of furosemide.
Famotidine + itraconazole (1)	D	Famotidine may decrease the serum concentration of itraconazole due to an increment in gastric pH.	Administer famotidine at least 2 h before or 2 h after itraconazole. Monitor patients closely for reduced itraconazole efficacy if combined.
Cyclosporine + mycophenolate (1)	D	Cyclosporine may decrease the serum concentration of mycophenolate.	Monitor mycophenolate dosing and response to therapy closely particularly when starting, stopping, or changing cyclosporine dose.
Ibuprofen or naproxen + furosemide (1)	D	Antagonistic/ ibuprofen may diminish the diuretic effect of furosemide.	Monitor patients for decreased therapeutic effect of furosemide.
Pantoprazole + itraconazole (1)	D	Absorption/ pantoprazole may decrease the serum concentration of itraconazole.	Administer itraconazole at least 2 h before or 2 h after itraconazole. Monitor patients closely for reduced itraconazole efficacy if combined.
Amlodipine + phenytoin (1)	D	Amlodipine may increase the serum concentration of phenytoin. Phenytoin may decrease the serum concentration of amlodipine.	Monitor for phenytoin toxicity. Monitor for reduced therapeutic effects of amlodipine.
Cyclosporine + atorvastatin (1)	X	Cyclosporine may increase the serum concentration of atorvastatin.	Avoid concomitant use of cyclosporine and atorvastatin. Consider changing to a statin that is less sensitive to this interaction. Limit the atorvastatin dose to no more than 10 mg daily.

Table modified from Hosseinpoor et al. (2022)

- Up to 63% of recently discharged medical-surgical patients had potential DDI when their drug charts were studied. Additional medication added in intensive care over their long-term meds will certainly increase the chance of DDI. As the number of medications used on each patient increases, the chances of drug–drug interactions rise exponentially.
- Use of proprietary interaction checkers (e.g., Micromedex, Lexi-Interact, etc.) in hospital prescription software increases the chances of timely alerts. However, excessive alerts, the need for frequent overrides, and "alert fatigue" must be considered before implementation.
- The top 25 DDIs involve several commonly used medications, including thyroxin, warfarin, digoxin, theophylline, fluoroquinolones, statins, phenytoin, benzodiazepines, fluconazole, clarithromycin, and MAO-inhibitors like linezolid.
- According to a study on signals to suspect DDIs, they should be considered when unexplained hypoglycemia, leucopenia, thrombocytopenia, low TSH, T4, elevated CPK, AST, or ALT, high INR or aPTT, high or low potassium, or hyponatremia occurs in any clinical setting.

Step 5b: Drug–Food Interactions

- Biochemical interactions between food and medications occur in ICU patients. For example, iron, calcium, milk, etc., can chelate all fluoroquinolones in the bowel and reduce their absorption.
- Fatty food increases absorption of itraconazole, but food reduces bioavailability of phenytoin and thyroxin significantly.

Step 5c: IV Line Piggyback Interactions

- As many ICU patients have maintenance IV fluids, adding any other medication can result in precipitation (calcium chloride + soda bicarbonate ➔ calcium carbonate), Ringer lactate (its calcium content) is incompatible with many medications like ceftriaxone, fluoroquinolones, imipenem, and blood products. Thus, by default, no medication should be added to Ringer's lactate or added to the line having Ringer's lactate.
- Amiodarone gets precipitated in normal saline at lower dilutions, so does phenytoin in dextrose-containing solutions.
- A list of drug dilutions must be fixed and followed as a protocol in intensive care.
- Involving clinical pharmacists while designing these protocols is highly desirable.

Step 6: Know Special Onset and Offset Kinetics of Key Drugs in ICU Patients

Step 6a: Context-Sensitive Half-Life

- In intensive care, many drugs are used as IV infusions for their immediate effects, but many have prolonged effects that last long after stopping their infusion—e.g., amiodarone (days to weeks), labetalol (5.5 h), insulin (2 h). Fat-soluble medications like fentanyl and midazolam when infused for hours in ICU patients get cumulated in fat and recirculated after stopping the infusions. This leads to the prolonged hangover effect of sedatives called context sensitive half-life, which is much longer than that of single boluses.
- Hydroxy-midazolam glucuronate, an active metabolite of midazolam, excreted by kidneys gets cumulated if the patient develops AKI during the use of midazolam infusions. This can account for undue prolonged sedation after stopping midazolam infusion and therefore should be avoided in patients with renal dysfunction.

Step 6b: Cautions in Antibiotic Infusions

PK-PD data: PK-PD of antibiotics vary according to their mode of action (killing or inhibiting growth of microbes) and can be grouped into one of the following three types. Time-dependent antibiotics are often used as prolonged infusions in the ICU; however, one needs to consider the limitations of this approach (Table 29.2).

There are limitations in the use of IV antibiotic infusions like IV piggyback incompatibility with other meds, post-dilution stability of antibiotics, etc. (Table 29.3).

Table 29.2 Antibiotic groups as per kinetics of killing

Concentration dependent (Cmax/MIC)	Time dependent (Time > MIC)	Concentration and time dependent (AUC—24h/MIC)
Gentamicin Amikacin Daptomycin Metronidazole	Piperacillin—tazobactam Meropenem Vancomycin Cephalosporins	Fluconazole Linezolid, Azithromycin Ciprofloxacin Glycopeptide Tigecycline

Table 29.3 Antibiotic stability after dilution at room temperature

Antibiotics	Stable at room temperature for Hours
Piperacillin, temocillin, aztreonam	At least 24 h
Ceftazidime	24 h at 25 °C, but only for 8 h, at 37 °c
Meropenem, doripenem, imipenem	3–4 h only
Amoxicillin	8 h
Penicillin	12 h

Modified from Van Herendael et al. (2012)

Step 7: Consider Therapeutic Drug Monitoring (Table 29.4)

- The dosing range defined by the manufacturer is often based on PK-PD on normal individuals and at times few lines of guidance for liver and renal dysfunction.
- Many medications have measurable therapeutic effects (BP, blood sugars, temperature, APTT, INR, etc.) but most don't (antibiotics, antiepileptics, thioxanthines, antibiotics). Therefore, periodic blood level monitoring is necessary.
- No specific guidance is available for ICU patients; however, timely achievement of therapeutic plasma concentrations (target tissue fluid concentration) and their maintenance is of vital importance in critically ill patients. Therefore, monitoring therapeutic drug concentrations, at least in a few critical situations (ECMO, CRRT, burns and trauma resuscitation, extremes of weight range, status epilepticus, etc.), is advisable, if not for all patients.

Availability of TDM and more importantly setting a minimal acceptable TAT are factors intensive care regimen has to consider and develop protocol accordingly (Table 29.4).

This step-by-step approach has led us to understand the following clarification on the etiology of the case vignette given above.

Table 29.4 Therapeutic drug concentrations

Drug	Therapeutic concentration	Toxic effects
Digoxin	Css: CHF: 0.5–0.9 ug/L AF: 0.8–2 ug/L (level measured 12 h after dose, or 24 hrs in CKD and HD patients)	Visual disturbance, dizziness, nausea and vomiting, PR prolongation, AV blocks, brady- and tachyarrhythmias (simultaneous thyroid function, potassium and magnesium check advised) <0.5 ug/L under digitalization, >1.2 ug/L increased mortality
Gentamicin, tobramycin	Cmax /MIC >8–10 Cmin <0.5 mg/L	Nephrotoxicity, ototoxicity
Amikacin	Cmax/MIC >8–10 Cmin <2.5 mg/L	Nephrotoxicity, ototoxicity
Vancomycin	Cmin >10 mg/L, >15–20 mg/L in severe infections. Css: 20–25 mg/L (continuous infusion)	Nephrotoxicity, ototoxicity, reversible neutropenia
Teicoplanin	Cmin >10–20 uncomplicated 20–30 mg/L severe complicated MRSA infections	Thrombocytopenia, neutropenia Cmin >60—nephrotoxicity
Phenytoin	Cmin: 10–20 mg/L	Nystagmus, ataxia, dysarthria, cardiovascular collapse Correct for hypalbuminemia Caution in uremia

(continued)

Table 29.4 (continued)

Drug	Therapeutic concentration	Toxic effects
Theophylline	Css: 10–20 mg/L (4 h after initiation infusion and 12 hourly)	Arrhythmia, nausea, vomiting
Beta-lactams	Css > MIC	Neurotoxicity at very high dose exposure
Daptomycin	AUC/MIC >666 Cmin (1 h before next dose) < 24 mg/L (72 h post-initiation)	Rhabdomyolysis (CPK—20-fold rise if Cmin > 24.3)
Linezolid	Cmin: 2–7 mg/L (48 h post-initiation)	Cmin 7–10/L—thrombocytopenia, neutropenia, serotonin syndrome
Colistin	Cmin: 2 mg/L, 48–72 h post-initiation	Nephrotoxicity, neurotoxicity
Polymyxin B	AUC 0–24:50–100 mg h/L	Nephrotoxicity, neurotoxicity
Voriconazole	Cmin: 2–6 mg/L (prophylaxis or treatment) 2–5 days post-initiation	Neuropsychiatric disturbances, visual disturbances, CYP C450 inhibition-associated interactions, cholestasis, poor oral bioavailability-related low levels
Posaconazole	Cmin >0.5–0.7 mg/L (prophylaxis) Cmin >1 mg/L (treatment) 7 days post-initiation	Nausea, vomiting

Modified from Antimicrobial therapeutic drug monitoring in critically ill adult patients: a Position Paper. Intensive Care Med. 2020 Jun; 46(6):1127–1153. *Cmin* 30 min or just before the next dose, *Cmax* 30 min after the end of infusion, *MIC* minimum inhibitory concentration for the microbe for that molecule, *Css* monitoring for continuous infusion, *AUC/MIC-based monitoring* two samples taken between 1.5 and 3 h post-dosing and the other one taken within 1 h of the next infusion, *AUC0-24* one sample taken between 12 and 24 h post-initiation of therapy

- Fasting has led to dehydration with a consequent drop in his renal function. His creatinine clearance was noted to have dropped from 25 ml/min to less than 10 ml/min now causing AKI. The interaction of dehydration (low renal blood flow), aceclofenac (NSAID—glomerular afferent vasoconstriction), and telmisartan (ARB—glomerular efferent vasodilatation) caused a further drop in glomerular filtration pressure and so GFR. This has led to the accumulation of atenolol causing hypotension and bradycardia, initiating a vicious cycle.

Thus, a step-wise approach from focused history-taking to revisiting pharmacological principles helps not only manage the patients in the ICU but diagnose the underlying etiology as well.

Suggested Reading

Abdul-Aziz MH, Alffenaar JC, Bassetti M, Infection Section of European Society of Intensive Care Medicine (ESICM), Pharmacokinetic/pharmacodynamic and Critically Ill Patient Study Groups of European Society of Clinical Microbiology and Infectious Diseases (ESCMID), Infectious Diseases Group of International Association of Therapeutic Drug Monitoring and Clinical Toxicology (IATDMCT); Infections in the ICU and Sepsis Working Group of International Society of Antimicrobial Chemotherapy (ISAC), et al. Antimicrobial therapeutic drug monitoring in critically ill adult patients: a position paper. Intensive Care Med. 2020;46(6):1127–53. https://doi.org/10.1007/s00134-020-06050-1. Epub 2020 May 7. PMID: 32383061; PMCID: PMC7223855. *An excellent resource for detailed PK-PD-based TDM recommendations for optimal antibiotic dosing in critical care patients.*

Bakker T, Abu-Hanna A, Dongelmans DA, et al. Clinically relevant potential drug-drug interactions in intensive care patients: a large retrospective observational multicenter study. J Crit Care. 2021;62:124–30. https://doi.org/10.1016/j.jcrc.2020.11.020. Epub 2020 Dec 1. PMID: 33352505. *DDIs in the ICU may be many but only half are clinically relevant; this study shows how to modify the clinical information support system in the ICU to reduce alert fatigue.*

Baxter K, Preston CL, editors. Stockley's drug interactions: a source book of interactions, their mechanisms, clinical importance and management hardcover. Pharmaceutical Press; 2012. *A source book of interactions.*

Budnitz DS, Lovegrove MC, Shehab N, Richards CL. Emergency hospitalizations for adverse drug events in older Americans. N Engl J Med. 2011;365:2002–12.

Glintborg B, Andersen SE, Dalhoff K. Drug-drug interactions among recently hospitalized patients—frequent but mostly clinically insignificant. Eur J Clin Pharmacol. 2005;61:675–81.

Goldberg RM, Mabee J, Chan L, Wong S. Drug-drug and drug-disease interactions in the ED: analysis of a high-risk population. Am J Emerg Med. 1996;14:447–50.

Hosseinpoor Z, Farzanegan B, Baniasadi S. Comparing important and well-documented potential drug–drug interactions between emergency, medical, and surgical ICUs of a respiratory referral center. Indian J Crit Care Med. 2022;26(5):574–8.

Malone DC, Abarca J, Hansten PD, et al. Identification of serious drug-drug interactions: results of the partnership to prevent drug-drug interactions. J Am Pharm Assoc (Wash). 2004;44:142–51. *The PP-DDI project is a major study funded by CDC that identified the 25 most important (common and relevant) DDIs in the whole pharmacopeia used during that era (2004).*

Smithburger PL, Kane-Gill SL, Seybert AL. Drug-drug interactions in cardiac and cardiothoracic intensive care units: an analysis of patients in an Academic Medical Centre in the US. Drug Saf. 2010;33(10):879–88. https://doi.org/10.2165/11532340-000000000-00000. PMID: 20812772. *Papers by Pamela Smithburger et al., from the University of Pittsburgh, are well-structured prospective studies in MICU, CCU, and CTICU by a dedicated clinical pharmacist to detect DDI in real-life case sheets.*

Smithburger PL, Kane-Gill SL, Seybert AL. Drug-drug interactions in the medical intensive care unit: an assessment of frequency, severity and the medications involved. Int J Pharm Pract. 2012;20(6):402–8. https://doi.org/10.1111/j.2042-7174.2012.00221.x. Epub 2012 Jun 7. PMID: 23134100.

Steven MH, et al. Consensus list of signals to detect potential adverse drug reactions in nursing homes. J Am Geriatr Soc. 2008;56(5):808–15. *This study lists the signals for one to suspect DDI in nursing homes but is relevant to clinical practice in general*

Van Herendael B, Jeurissen A, Tulkens PM, Vlieghe E, Verbrugghe W, Jorens PG, Ieven M. Continuous infusion of antibiotics in the critically ill: the new holy grail for beta-lactams and vancomycin? Ann Intensive Care. 2012;2(1):22. https://doi.org/10.1186/2110-5820-2-22. PMID: 22747633; PMCID: PMC3532155. *Good read about post-dilution drug stability for antibiotic infusions in the ICU.*

Safety and Drug Errors in the ICU

30

Ritesh Shah and Anuj M. Clerk

Case 1

A 56-year-old male, a known case of diabetes mellitus and ischemic heart disease, presented with bilateral pneumonia complicated by ARDS and septic shock. He was on invasive ventilation with 85% FiO_2 and receiving a high-dose noradrenaline infusion. At 4 am, during sponging, the patient's central venous access was accidentally dislodged. He subsequently suffered a cardiac arrest. CPR was performed, and he was successfully revived. However, the patient sustained significant hypoxic brain and cardiac damage.

Case 2

A 46-year-old female, a known case of hypertension, was admitted to the ICU for angina and was gradually recovering. During oral medication administration, the patient was mistakenly given Tab. Metoprolol 50 mg twice a day instead of the prescribed 25 mg twice a day. This resulted in significant hypotension with bradycardia, requiring vasopressor infusion.

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Case 3

A 67-year-old female with diabetes was admitted at 11 am with urosepsis and septic shock. Blood cultures were ordered, and antibiotics were prescribed with a thrice-daily dosing regimen. However, the first dose of antibiotics was administered at 2 pm due to the routine practice of giving medications prescribed for thrice-daily dosing at fixed times: 2 pm–10 pm–6 am.

The article "To err is human: Building a safer health system", published in the year 2000 by the Institute of Medicine (US) Committee on Quality of Health Care in America, discussed the importance of errors in healthcare as they can result in significant increase in mortality, morbidity, and the financial burden to the family and the institute. It also increases the emotional burden on the family members and the healthcare workers. As per the WHO report (2023), more than 3 million deaths occur annually due to unsafe care. This is much more than the commonly perceived causes of death including road traffic accidents, malignancy, etc. Around 1 in every 10 patients is harmed in healthcare while more than 50% is preventable. Out of all the medical errors, about two-thirds are medication errors. This is probably because of less awareness, underreporting, and less research.

Step 1: Understand the Concept of Safety

Safety and quality are integral parts of patient care. Unintentional errors result in compromising safety. By preventing medical errors, patient safety and thereby quality improves. Because of its nature, ICU is more prone to errors and suffers more serious adverse consequences. We can't have an error-proof care provider, but we can create a safety culture by creating an error-proof environment by making and following systems, protocols, etc. This originates from the Hippocratic Oath "primum non nocere"—"First do no harm."

Step 2: Familiarize the Terminologies

There are lots of terms that are used interchangeably, but there are definite differences between them (Table 30.1).

Table 30.1 Terminologies

Patient safety	The avoidance, prevention, and amelioration of adverse outcomes or injuries stemming from the process of healthcare.
Slips/lapses	Errors when executing a correctly planned action. Slips are due to errors in performing the action and lapses are due to failing in performing the action.
Mistakes	Errors in planning actions.
Near miss	Any event that could have had an adverse patient consequence but did not result in a poor outcome.
Incident	Unexpected or unanticipated events or circumstances, not consistent with the routine care of a particular patient, which could have, or did lead to, an unintended or unnecessary harm to a person, or a complaint, loss, or damage.
Adverse event	Unintended injury or complication to patients that results in measurable disability, death, or prolonged hospitalization.
Medical error	An act of omission or commission in planning or execution that contributes or could contribute to an unintended result.
Prescription error	Failure of the process of prescription writing/documentation that results in wrong instruction about one or more of the normal features of a prescription, like dose, duration, dilution, date, frequency, etc.
Medication error	Any preventable event that may cause or lead to inappropriate medication use or patient harm, while the medication is in the control of the healthcare professional, patient, or consumer.
Sentinel event	An unexpected occurrence involving death, serious physical or psychological injury, or the risk thereof

Step 3: Understand the Progression of the Error

The progression is usually from the incidence to near miss to ultimately an error. James Reason proposed a “Swiss cheese model of error causation.” It gives insight into the error occurrence. He suggested that most complex systems (like Intensive Care Units) and work environments (stressful ones like ICU) have different layers of defense. Consider each layer (of the system) is a slice of Swiss cheese (Fig. 30.1). Each layer (system) always possesses several holes or flaws as no system is perfect. There are times or circumstances or “opportunities” when these holes align together in such a way that bypass all layers of defense resulting in an error.

The errors occur due to active failures (because of skill or knowledge-based errors) or latent conditions in the presence of some situational factors (like fatigue, distraction, multitasking, etc.).

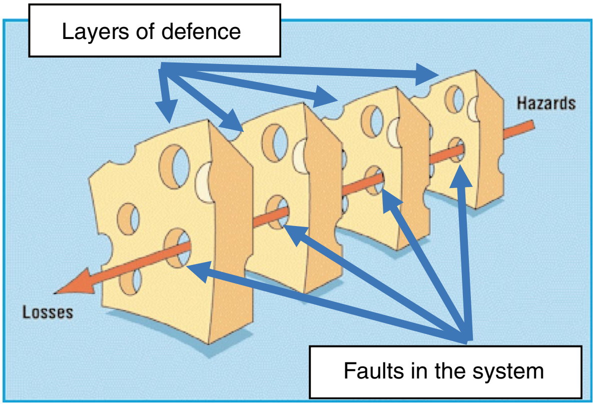

Fig. 30.1 Swiss cheese model. (Modified from Reason 2000)

Step 4: Evaluate the Reasons for Error Underreporting

More commonly, there is no working culture for reporting errors for fear of disciplinary actions. There is a tendency to hide the error. The common practice is to find out "WHO" is at fault rather than "WHAT" is at fault. Because of this, the same error tends to be repeated and sometimes it may lead to unintended consequences. Furthermore, very few hospitals have error reporting systems and transparency in documentation. There is very little participation (if at all any) in the study of errors at large scale because of the fear of getting defamed when published, despite the confidentiality status.

Step 5: Identify the Factors in the ICU That Contribute to Errors

- Multiple caregivers
- Too many experts involved in the care
- Complex disease
- Multiple organ involvement
- Less time for decision-making
- Multiple medications
- More frequent changes in the treatment plan
- Stressful environment
- Severity of illness
- Multiple intervention
- Deficit of trained manpower
- High turnover of patients
- Multiple emergency admissions
- An Intensivist needs to be a multi-tasker while managing critically ill patients, e.g., to do a procedure, train nurses, counsel family members, co-ordinate/liaise with multiple departments/consultants, etc.
- High attrition rate of caregivers

Step 6: Identify the Probable Reasons for Drug Errors in the ICU (Table 30.2)

The process of medication starts from prescription to transcription to dispensing to preparing to administer. There are a lot of scopes of making an error, especially in the ICU. Approximately 1.2–947 errors per 1000 patient days occur in ICUs, which may be 2–3 times more hazardous in critically ill patients and 2.5 times more likely to be fatal as compared to non-critically ill stable patients.

Table 30.2 Probable reasons for drug errors in the ICU

Probable reasons of drug errors in the ICU over and above the general factors	
Medication related	Patient related
Use of a higher number of drugs Drug–drug and drug–food interactions	Severity of illness The higher the severity, the higher the chances of ADE
Spelling errors	Requirement of high-risk medications
Illegible handwriting when hand-written	Extremes of ages—require special attention
No standardization in prescription writing No capital letters in writing prescription No capital letters in writing the dosage frequency like TDS vs TDS No standard format tds vs tid No order maintained about writing drug name, dose, frequency, dilution, duration of administration, route of administration, etc. Multiple formats used as per convenience and habits No pharmacological name of the drug written Multiple look-alike sound-alike brand names which are different compounds Decimal errors (zero point one .1, read as 1, 1.0 read as 10), “l” read as one (Paracetamol 500 as Paracetamol 1500), “U” misread as Zero (Insulin 2 Units as 20 Units)	No or minimal, patient participation in the care makes them vulnerable to error Poor organ reserves to tolerate any additional insult
No repeated review of the drug chart by the doctor, especially when no change in the drug chart for 2–3 consecutive days	Prolonged/repeated hospitalization—higher chances of ADE
Calculation-based errors Wrong weight-based calculation as most of the time it is calculated as predicted body weight Wrong calculation when the drug is diluted Wrong infusion rate	Dosing errors because of altered pK/pD In liver or renal dysfunction resulting in relative drug overdose Relative drug underdose in the case of augmented renal clearance Extremes of age requiring special dosing attention
Labeling errors	Allergy related issues
Wrong combination of drugs	
Frequent use of drug boluses or infusions	

In the ICU, the above are the probable reasons that are likely to contribute to an error occurrence over and above the general factors:

Moreover, there are certain errors that are not recognized and tend to be repeatedly occurring. This is because there is no formal education for the same. As we discussed in our cases, these kinds of errors are very common and need to be addressed seriously.

Step 7: Adapt Tools to Measure Safety

Various systems and tools are available to measure safety in the hospital. A few of them are described in Table 30.3.

Table 30.3 Tools to measure safety

Tool	Description	Pro and Cons
Incident report system	Evaluation of a single incidence where the harm occurred E.g., ISMP (Institute for Safe Medication Practices) Error Reporting System	Voluntary Anonymous Not punishable Try to find out "what" is at fault rather than "who" is at fault Analyze the root cause and formulate the action plan to prevent the same incident in the future
Root cause analysis	More focused evaluation of certain incidents	Implement preventive measures
Failure mode and effect analysis	Identify error-prone processes	Multidisciplinary team to implement prospective actions
ICU audits	Prepare guidelines/protocols based on national or international guidelines Compliance audit	By internal or external agencies and maintaining transparency
Trigger tools or targeted injury detection systems	A strategy to detect safety hazards to prevent harm	Retrospective analysis of medical records to identify SA/SAE, its frequency Compliance/progress of safety protocols
Process of care measurement	Evidence-based action or intervention Measures the compliance/adherence to the best patient care practices/protocols	Analyze discharge summary Retrospective chart review Automated surveillance Voluntary incident/error reporting system

Step 8: Implement Strategies for Medication Safety

There are five fundamental questions to be asked while patient care is ongoing.

1. Has patient care been safe in the past?
2. Are our clinical systems and processes reliable? It reflects the reliability.
3. Are we responding and improving? It reflects integration and learning.
4. Is care safe today? It reflects sensitivity to the ongoing operation.
5. Will care be safe in the future? It reflects anticipation and preparedness.

Strategies

Improvement in medication safety can be done by improving the processes, understanding the situational factors, and using advanced technology. There are lots of systems/strategies to prevent drug errors and thereby improve the safety of patients (Table 30.4).

Table 30.4 Strategies to prevent medical errors

Optimization of medications process		
Medication standardization	Use of standard drug concentration charts Use of user-friendly labels Standardized format of prescription	Advantages: Can be customized as per unit-specific requirements The labels can be prepared in local language Disadvantages: Needs chart reference majority of the time The chart should be available in multiple places
Computerized physician order entry (CPOE)	Involves prescription and transcription stages of the medication process Allow direct order entry into the computer, which is connected to HIS (hospital information system)	Advantages Can track documented allergies Suggests the dosage and dosage adjustments in organ dysfunction Gives an indication of the significant drug–drug interaction Less chances of look-alike-sound-alike drug-related errors as it also mentions the drug's pharmacological name Disadvantages : Costly systems Needs technical update from time-to-time Evidence of paradoxical increase in errors while in the implementation phase Time-consuming at the initial stages

(continued)

Table 30.4 (continued)

Optimization of medications process		
Use of barcode technology	Involves the administration stage of the medication process Usually used along with CPOE Labels the patient, the drug, and the administering person and document these electronically	Advantages: Ensures: Right patient Right drug Right dose Right dilution Right route of administration Right duration of administration Right time Disadvantages: Cost
Use of computerized syringe and volumetric infusion pumps	Allow incorporation of CPOE and barcode technology	Advantages We can feed the standard drug concentration Can suggest the drug infusion rate Can set the dose limits Gives alarms if any interruption or when approaching finishing the syringe volume, thereby avoiding any drug-interruption duration (important for drugs like vasopressors) Disadvantages : Cost Require calibration from time-to-time
Medication reconciliation programs	Incorporates patient's long-term medications, which are often forgotten after admission to ICU and later not re-started	Advantages Prevents medication withdrawal and its consequences

1. Minimize situational risk factors		2. Other error-preventing strategies	
Avoid the long/cumulative working hours	Avoid double shifts working Assign duty in such a way that balances the risk of care provider fatigue and the risk of frequent patient hand-over	Intensivist Participation	Minimized errors
Manage the stressful environment	Keep on engaging the case provider in various stress-buster activities Encourage them with reward programs including error-reporting reward programs	Pharmacist participation	Pharmacovigilance helps prevent errors
Graduated responsibility	The transition from trainee supervision to graduated responsibility needs to be managed efficiently Avoid giving multiple tasks to less experienced care providers	Adequate nurse–patient ratio	Proper distribution of nurse:patient as per the patient's condition and support

(continued)

Table 30.4 (continued)

1. Minimize situational risk factors		2. Other error-preventing strategies	
Avoid the long/cumulative working hours	Avoid double shifts working Assign duty in such a way that balances the risk of care provider fatigue and the risk of frequent patient hand-over	Error reporting reward programs	Encourages the care provider to report errors
Manage the stressful environment	Keep on engaging the care provider in various stress-buster activities Encourage them with reward programs including error-reporting reward programs	Educational programs	Talk more about errors, importance of reporting and prevention programs
Graduated responsibility	The transition from trainee supervision to graduated responsibility needs to be managed efficiently Avoid giving multiple tasks to less experienced care providers	Innovative programs	Error prevention modules

Step 9: Use the Innovative Approach of Error Prevention Modules

We can design innovative programs and workshops especially to recognize errors early and prepare preventive modules. One such program can incorporate labeling the errors that keep on happening in the ICU, are never documented, are not acted upon, and thereby become vulnerable to the recurrence of the same error. These errors are not mentioned in one place in the literature but are witnessed very routinely. These errors are even unit-specific, area-specific, manpower-specific, system-specific, etc. We can identify these errors by making criteria of the individual error, making care providers aware of the circumstances in which it occurs, giving these errors innovative and fancy names so that it is easy to remember, and doing awareness campaigns or workshops to educate further.

Here are a few examples:

1. Sponging Syndrome:

As discussed in case 1, the accidental removal of central venous access and its dangerous consequences are not uncommon. These disasters do occur during the sponging time, which is usually between 4 and 7 am. We can label it “sponging syndrome” and label the precautions like care of tubes and lines, witnessing the sponging of high-risk patients by on-duty doctors, delaying the sponging of most risky patients during daytime in the presence of the bigger team, etc. This awareness can be created easily and most effectively by this terminology. You need to just instruct—“Pl take care of sponging syndrome” and daytime sponging of the XYZ patients. This definitely prevents errors from occurring during this vulnerable time.

2. Look-Alike-Dose-Alike (LADA Syndrome) Medications:

In the second case, Tab Metoprolol was accidentally administered in a double dose because the difference between 25 mg and 50 mg was missed. While look-alike-sound-alike (LASA) or sound-alike-look-alike drug (SALAD) errors are well known, there is another common risk in ICUs. Many drug strips of the same medication but with different strengths look almost identical (e.g., metoprolol 25 mg vs. metoprolol 50 mg). This error is more common during dose titration (either up or down) than with LASA drugs. To address this, we can introduce the term “look-alike-dose-alike (LADA) drugs,” which highlights the risk of confusing different strengths of the same medication.

3. 2–10–6 Syndrome:

In the third case, the first dose of the antibiotic was delayed by three hours due to the routine practice in many ICUs/hospitals of administering TDS doses at fixed times: 2 pm–10 pm–6 am. Although this schedule is convenient for staff, it can lead to clinically significant delays, especially in critical care settings. In cases of sepsis or severe infections, even a 3–4 h delay in antibiotic administration can increase mortality and worsen outcomes. Despite repeated reminders, this fixed-timing practice persists in many ICUs. To raise awareness and encourage prompt action, we can introduce the term “2–10–6 syndrome,” which captures this systemic delay in a memorable way. The unique and catchy name makes it easy to remember and may help reinforce the need for timely antibiotic administration without requiring constant reminders.

ICUs are highly complex environments where various types of errors frequently occur, including medication errors, system-related errors, communication errors, transportation-related errors, and procedure-related errors. To reduce ICU errors, we can implement an innovative, multifaceted approach.

Step 10: The Safety Culture and Drug Error Prevention Programs

Hospitals should designate a dedicated quality and safety leader to collaborate with the ICU team. Staff members should be engaged through motivational methods rather than punitive measures. The adoption of computer-based, particularly AI-powered, systems can significantly enhance safety. Additionally, innovative and customized programs should be designed and effectively implemented.

References

Aronson JK. Medication errors: what they are, how they happen, and how to avoid them. Q J Med. 2009;102:513–21. https://doi.org/10.1093/qjmed/hcp052.

Grober ED, Bohnen JMA. Defining medical error. Can J Surg. 2005;48(1)

Institute of Medicine (US) Committee on Quality of Health Care in America. To Err is human: building a safer health system. Kohn LT, Corrigan JM, Donaldson MS, editors. Washington, DC: National Academies Press (US). 2000. *Original article on errors in healthcare.*

Juneja D, Mishra A. Medication prescription errors in intensive care unit: an avoidable menace. Indian J Crit Care Med. 2022;26(5):539–40.

Leape LL, Brennan TA, Laird N, Lawthers AG, Localio AR, Barnes BA, et al. The nature of adverse events in hospitalized patients: results of the Harvard Medical Practice Study II. N Engl J Med. 1991;324:377–84.

Measurement of Patient Safety. PSNet [internet]. Rockville: Agency for Healthcare Research and Quality, US Department of Health and Human Services. 2019. https://psnet.ahrq.gov/primer/measurement-patient-safety

Moyen E, Camiré E, Stelfox HT. Clinical review: medication errors in critical care. Crit Care. 2008;12:208. https://doi.org/10.1186/cc6813.

NCCMERP. The national coordinating council for medication error reporting and prevention. Medication errors—definition. Available at: https://www.nccmerp.org/about-medication-errors. Accessed on 10 Aug 2024.

Rangnathan N, Rungta N, Govil D, Munjal M, et al. Quality indicators in ICU, ISCCM. 2009

Reason J. Human error: models and management. BMJ. 2000;320:768–70. Describes the Swiss Cheese effect

Slawomirski L, Klazinga N. The economics of patient safety: from analysis to action. Paris: Organisation for Economic Co-operation and Development; 2020, assessed from World Health Organization/patient safety. *WHO report on healthcare safety.*

Triggers and Trigger Tools. PSNet [internet]. Rockville: Agency for Healthcare Research and Quality, US Department of Health and Human Services. 2019. https://psnet.ahrq.gov/primer/triggers-and-trigger-tools

Vincent C, Burnett S, Carthey J. Safety measurement and monitoring in healthcare: a framework to guide clinical teams and healthcare organisations in maintaining safety. BMJ Qual Saf. 2014;23:670–7.

Transportation of Critically Ill Patients

31

Subhankar Paul and Rajesh Pande

Case Vignette

A 57-year-old male patient was admitted to the emergency department of a small hospital with complaints of chest pain and palpitation. He was found to be hypotensive with inferior wall STEMI, pulmonary edema, and a low ejection fraction of 30%. The patient was initially given NIV but was later intubated and put on invasive ventilation. The hospital did not have a Cardiac Cath lab. The cardiologist resuscitated the patient and administered thrombolysis. The patient was subsequently sent to a higher center for PCI interventions and further care. The patient was on 10 ml/h of noradrenaline infusion and ventilatory support. He was shifted to an ACLS ambulance.

Inter- and intrahospital transport is commonly undertaken for critically ill patients requiring advanced diagnostics, major interventions, and advanced medical/surgical care. Victims of major roadside trauma may require on-site stabilization and quick transfer to a trauma center. These critically ill patients are in a dynamic and vulnerable physiological state and the transport process potentially exposes them to additional harm, instability, and increased risk of morbidity and mortality during transport.

A protocolized approach that includes planning, preparation, standard monitoring, liberal communication, appropriate documentation, and use of experienced manpower during transport is essential for the safe transport of critically ill patients.

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The ideal way to consider the transport of a critically ill patient is as a “mobile ICU environment.”

Types of Transport

Transfer of critically ill patients is performed for multiple indications (Table 31.1) by healthcare professionals using various platforms. Broadly, patient transfers can be categorized by:

- Based on level of care: primary, secondary, tertiary
- Urgency of care: emergency, urgent, routine
- Indication for transfer: clinical or capacity (triaging)
- Transfer platform: bed, road, or air
- Level of care required during transit:
  - Level 0: Stable patients in the ward and not required to be accompanied by specialized personnel.
  - Level I: Patients at risk of deterioration during transport and should be accompanied by a trained paramedic or nurse.
  - Level II: Patients requiring continuous observation and interventions for single organ failure and should be accompanied by a competent physician.

Table 31.1 Commonly used transfer terms

Primary transfer	Movement of patients from the scene of injury or illness, to the nearest receiving hospital
Extended primary transfer	Movement of a patient from the scene of injury or illness to a specialist center or trauma center, bypassing the nearest hospital to reach a center more appropriate to the needs of the patient
Secondary transfer	Movement of a patient from any hospital facility (emergency department/ward/critical care unit/operating theatre) to another center
“Clinical” transfer	Patient transfer for specialty treatment or investigation not provided at the referring hospital
“Capacity” transfer	Patient transfer for specialist treatment or investigation normally provided at the referring hospital, but this is not currently available
Repatriation	Patient transferred back to the referring hospital or a hospital nearer the patient’s home
Interhospital transfer	Transfer of a patient between hospitals
Intrahospital transfer	Transfer of a patient between areas/departments within the same hospital site
Primary ECMO transportation	A mobile ECMO team initiates ECMO at an outside facility and, after initial stabilization, the patient is transferred to an ECMO center
Secondary ECMO transportation	A patient is currently supported with ECMO but must be transferred to another facility on ECMO support
Tertiary ECMO transportation	Hospital A has a patient with an ECMO indication and a mobile ECMO team from Hospital B goes to Hospital A. The ECMO team from Hospital B puts the patient on ECMO and transports the patient to Hospital C with ECMO capacity
Intra-facility ECMO transfer	A patient is currently supported with ECMO but must be moved within an institution

  - Level III: Patients on mechanical ventilation with 2 organ failures and must be accompanied by competent physicians, besides paramedic and nursing staff.
- Distance/duration of transfer: intrahospital, interhospital, or international transfer

Intrahospital Transport

Step 1: Evaluate the Need for Transport

- The most important initial step is to evaluate the potential benefit that may be derived by shifting the patient against the risks involved.
- The purpose and the justification for transport should be noted in the case sheet.
- The potential risks can be minimized by careful planning of the procedure and utilization of available equipment and personnel.
- The timing of transport should also be carefully decided, preferably during day time for elective transfers.
- A multidisciplinary team of physicians, nurses, paramedical staff, and transport coordinators is required to plan and coordinate the process.

Step 2: Identify High-Risk Patients

- Patients in the following categories are at particularly high risk for deterioration during or after transport:
- The mechanically ventilated patients, particularly those with the requirement of high PEEP >6 and FiO_2 more than 0.5. Extra oxygen reserve for patients with high oxygen requirements should be kept.
- Patients with higher injury severity.
- Patients with traumatic brain injury.
- Hemodynamically unstable patients requiring continuous infusion of single/multiple vasoactive drugs—noradrenaline, vasopressin, adrenaline, dobutamine, etc.

- *Transport of the patient should not be undertaken in the following circumstances:*
  - If there is any predicted inability to maintain airway control, breathing (oxygenation and ventilation), or circulatory parameters, or to adequately monitor the cardiopulmonary status during transport or at destination.
  - If all the necessary members of the transport team are not present.
  - If the receiving team is not ready.

- *Decision*: Transporting a patient in serious condition is a critical decision and should involve the senior physicians in the unit.

Step 3: Pre-transport Coordinate and Communicate

- Effective communication should be established between physician-to-physician, nurse-to-nurse, and the service/therapy provider to reduce transit time and delays.
- The clinical condition and the urgency for the study or therapy should be discussed to avoid waiting.
- The receiving team should signal their readiness to receive the patient for immediate procedure and testing.
- Patients/relatives are to be counseled regarding the need for transport and any risk involved.

Step 4: Decide Accompanying Personnel

- All critical transfers should be accompanied by a physician (preferably from the treating team), nurse, and a paramedic with full resuscitation gear including equipment and medications.
- It is strongly recommended that a physician competent in airway management and advanced cardiac life support accompany the unstable patient.
- Additional help may be asked from the ICU if the situation demands so.
- The transport personnel should accompany the patient until return to the ICU.

Step 5: Decide the Equipment Required

- The equipment to be used during transport should be dedicated and should not be used anywhere else.
- A transport monitor including ECG, heart rate monitor, blood pressure monitor, pulse oximeter, invasive and/or noninvasive ventilators, and defibrillators.
- Basic resuscitation drugs, including epinephrine, norepinephrine, antiarrhythmic drugs, vasopressin, muscle relaxants, sedatives, narcotics, analgesics, dextrose ampoule, and appropriate IV fluids.
- Intubation and resuscitation equipment for ACLS.
- Drip medications properly labeled must accompany the patient.
- All battery-operated equipment must be fully charged and should have adequate battery backup provision.
- Portable oxygen to cover the transport duration with an additional reserve of 30 min.
- The portable ventilator should have control and spontaneous modes, FiO_2 up to 100%, PEEP and airway pressure, and disconnection alarms.
- In mechanically ventilated patients, endotracheal tube position is noted and secured before and during transport and the adequacy of oxygenation and ventilation is reconfirmed.
- No equipment or drugs should be placed over the patient. Most units will have custom-made shelves, which will fit on the beds or trolleys.

- The monitors and/or ventilators should be properly secured with straps to the bed or shelves so that they do not fall on the patient.

Step 6: Monitoring During Transport of Critically Ill Patients

- Monitoring should continue during the transport as well as inside therapy or diagnostic areas:
  - Continuous ECG monitoring
  - Continuous pulse oximetry
  - Periodic measurement of the blood pressure, pulse rate, and respiratory rate
  - Selective patients may benefit from capnography, continuous intra-arterial blood pressure monitoring, and intracranial pressure monitoring if required.

Step 7: Take Care During Transport

- Ideally, the patient should receive the same level of care as in the ICU.
- Vital signs must be monitored and recorded at intervals.
- Use of memory-capable multipara monitors is recommended. This will allow documentation of data during transport.
- Any adverse events should be noted and immediately managed.
- There should be a designated senior physician available for consultation in the case of an adverse or critical event during transport. Ideally, he/she should be available on-site and should be able to arrive at the destination area if required.
- The transport team should be able to communicate with the designated person during transit as well as upon arrival at the destination in the case of an emergency.

Step 8: Do Documentation

- Documentation in the medical record should be done, which includes the following:
  - Indication of transport
  - Clinical status of the patient before, during, and after return to the ICU
  - Any critical event during the whole process
  - Signature of the transport team personnel

Interhospital Transport

Basic requirements are the same for intra- or interhospital transport. However, interhospital transport requires more planning, more personnel, consideration of the choice of vehicle and its availability, altitude effects in air transport, weather conditions, battery life of equipment, backup equipment, oxygen supply, power supply, a contingency plan in the case of breakdown, and more documentation for medicolegal purposes.

Step 1: Take Informed Consent

- Informed consent for interhospital transport must be taken from a competent patient, or from a guardian/legally authorized representative if the patient is incompetent.
- It includes a discussion of the risks and benefits of transfer and its documentation in medical records before transfer.
- In the case of life-threatening emergencies when an informed consent cannot be taken, the indication of transfer and the reason for not obtaining consent must be documented.

Step 2: Plan, Communicate, and Coordinate Before Transport

The transport action plan carried out by the transport team should consider the following issues:

- The referring physician will contact the receiving physician and will explain the clinical condition to him/her.
- *Choice of mode of transport*: Air or road will be determined by the transferring physicians based on the medical condition, time savings, available facilities, and required medical interventions. Air transfer may be considered for longer journeys of more than 80 km or 2 h. Helicopters are recommended for journeys of 80–240 km or if access is difficult. Fixed-wing pressurized aircraft should be used for transfer distances over 240 km. The advantages and disadvantages of individual modes are discussed in Table 31.2.
- Choosing the monitoring and other support equipment.
- Anticipating potential complications during transport and necessary steps to prevent/tackle such complications.
- Choice of transport team as per the condition of the patient and available resources.

Step 3: Prepare the Patient

Appropriate preparation of the patient before transfer is crucial for preventing problems and delays. A systematic approach (e.g., “airway, breathing, circulation (ABC)” or similar) helps to avoid oversight and pre-empt potential pitfalls.

- A patient should only be transported after airway stabilization if airway patency is anticipated to become an issue during transport. It is difficult to

Table 31.2 Advantages and disadvantages of different modes of transport

Mode of transport	Advantages	Disadvantages
Road ambulance	Quickest to arrange Cheaper No altitude-related issues Less affected by inclement weather If needed, the ability to pull over to perform a lifesaving procedure	Limited range Limited speed Clear road access needed Much more vibrations, depending on the road conditions
Helicopter	Faster to organize than fixed-wing aircraft Rapid transit time Being a vertical take-off and landing (*VTOL*) aircraft does not need an airport/runway Less turbulence than a road ambulance	Range is limited Expensive Highly weather-dependent Small cabin, limited space Noisy for crew and patient Communication possible only via headset Cabin not pressurized; mild complications of high altitude possible Poorer safety records
Fixed-wing aircraft	Highest range Fastest speed Less weather dependent than a helicopter Large cabin, more space for equipment and crew Better temperature and noise control than a helicopter Can be pressurized at high altitude	Most expensive Slowest to organize Need to load into an ambulance, then into aircraft at the airport, then disembark at another airport and load into another ambulance (i.e., tantamount to three separate transfers)

intubate a patient in a moving ambulance as the conditions are suboptimal. The endotracheal tube should be properly secured to avoid dislodgement during transport.

- Any pneumothorax should be drained beforehand. Oxygen saturation and end-tidal CO_2 monitoring should continue en route. It is suggested that the oxygen requirement during transport should be twice the patient and ventilator oxygen consumption. The transport ventilator should have provision for spontaneous breathing, disconnection, and high-pressure alarms with adequate battery backup.
- Fluid resuscitation and vasopressor support should be initiated before transport if required. Good venous access, preferably a jugular or subclavian central venous catheter or two large bore peripheral cannulas, should be obtained. Blood products should be arranged beforehand if the need is anticipated during transport. The need for special equipment like an intra-aortic balloon pump, cardiac pacing, and intracranial pressure monitoring should be anticipated and arranged before initiating transport.
- The trauma patient should be immobilized, secured, and well-covered.

- Vascular access lines, drains, and indwelling catheters should be secured in place, and if a nasogastric tube or urinary catheter is required, it should be inserted.
- In critical transfers, it is advisable to use neuromuscular blockers, sedatives, and analgesics to achieve stability en route.
- Transfer trolleys must be secured tightly into the vehicle to protect the patient and transfer team in the case of an unprecedented accident.
- A copy of the medical record including case summary and all relevant laboratory and radiographic data will accompany the patient.

Step 4: Decide on Accompanying Personnel

- The transport team should have a minimum of two members besides the driver. The critical transfers must be accompanied by experienced intensivists and nurses who are competent to handle en route medical emergencies like advanced airway, arrhythmias interpretation, basic and advanced cardiac life support, and other lifesaving interventions.
- The transport team leader should be a treating physician/intensivist/anesthesiologist/emergency physician with additional training in transport medicine.
- Super-specialist services may often be required for pediatric transfers and for patients on IABP or ECMO.
- The transport personnel will remain with the patient until reaching the ICU.
- There must be a clear chain of responsibility throughout the transfer. A proper handover from the referring physician to the transfer physician and then to the receiving facility physician is essential.

Step 5: Choose Transport Equipment and Medicines

- When choosing the equipment, the following should be considered: size, weight, battery life, ability to fit trolley railings, ability to function under conditions of vibration, ease of use in poor light, and placement in restricted space.
- Equipment should be adequately restrained and should be easily accessible to the operator.
- Backup equipment may be desirable in some situations.
- The recommended minimum transport equipment and medications are given in Table 31.3.
- Additional drugs like scheduled dosages of antibiotics, antiarrhythmics, or others should be taken along with those that need to be dosed during transport.
- It is a good idea to have a pre-departure checklist to avoid any critical shortcomings during critical transfers as their use has shown significant improvement in safety during transport. A sample checklist has been given in Table 31.4.

Table 31.3 Recommended minimum transport equipment and medications

Equipment	Medications
Airway management—adult and pediatric	*Respiratory and rapid sequence intubation medications*
Macintosh, Miller and McCoy laryngoscope blades—all sizes Laryngoscope handles (adult and pediatric) Extra laryngoscope batteries and light bulbs Endotracheal tube stylets (adult and pediatric) Magil forceps (adult and pediatric) Cuffed endotracheal tubes (5.0–8.0) Uncuffed endotracheal tubes (2.5–5.0) Nasopharyngeal airways (assorted sizes) Oral airways (#0, #1, #2, #3, #4) LMA 2,3,4 Combi tube 41F Scalpels with blade for cricothyroidotomy Needle cricothyroidotomy kit Percutaneous tracheostomy set Cuff pressure gauze Water-soluble lubricant Adhesive tape Heimlich valve Suction apparatus Suction catheters (#5, #8, #10, #14)	Pretreatment agents (midazolam, fentanyl) Induction agents (propofol, etomidate, ketamine) Neuromuscular blocking agents (succinylcholine, rocuronium, atracurium) Salbutamol respules, 2.5 mg/2.5 ml Budesonide respules, 0.5 mg/2 ml Terbutaline, 1 mg/1 ml Methylprednisolone, 125 mg/2 ml

(continued)

Table 31.3 (continued)

Equipment	Medications
Breathing equipment	*Fluid and electrolytes*
Adult and pediatric self-inflating resuscitation bag-valve systems with oxygen reservoir and masks (assorted sizes)	Calcium gluconate, 1 g/10 ml
	Potassium chloride, 20 meq/10 ml
Bain circuit (adult), C circuit (adult), pediatric circuit	Magnesium sulfate, 1 g/2 ml
Flexible adaptors to connect bag-valve system to endotracheal/tracheostomy tube	Dextrose 25%, 100 ml
End-tidal carbon dioxide monitors (pediatric and adult)	Intravenous solutions (plastic bags)
Infant medium- and high-concentration masks with tubing	1000 ml, 500 ml of normal saline
Nasal prongs, face mask, face mask with nebulizer, non-rebreathing mask, NIV mask	1000 ml of Ringers lactate
	500 ml of 5% dextrose
Ventilator circuit (adult and pediatric)	Sodium bicarbonate (8.4%), 25 ml/50 ml
Heat moisture exchange filter (HME), bacteria viral filter (BVF)	Sterile water, 30 ml for injection
Transport ventilator	Glucagon, 1 mg vial (powder) Miscellaneous (as per need)
Aerosol medication delivery system (nebulizer)	Narcotic analgesics (e.g., morphine, fentanyl)
	Naloxone, 2 mg/2 ml
	Sedatives/hypnotics (e.g., lorazepam, midazolam)
	Anticonvulsants (phenytoin, levetiracetam, Phenobarbital)
	Antihistaminic (promethazine/ pheniramine)
	Mannitol (20%), 100 ml
	Prostaglandin E1, pulmonary surfactant (special circumstances)

Circulation equipment Intravenous catheters, sizes 16–24-gauge Intravenous fluid administration tubing Blood administration tubing Extension tubing Infusion pumps Pressure bags for fluid administration Bone marrow needle (for pediatric infusion) Butterfly needles (23-gauge, 25-gauge) Hypodermic syringes, assorted sizes (2 ml, 5 ml, 10 ml, 20 ml, 50 ml) Hypodermic needles and syringes, assorted sizes Three-way stopcocks Tourniquets for venepuncture/IV access Arterial line tubing ECG electrodes (infant, pediatric, adult) Defibrillator electrolyte pads or jelly ECG monitor/defibrillator (preferably with pressure transducer capabilities) Transcutaneous pacemaker	*Cardiac* Adenosine, 6 mg/2 ml Amiodarone, 150 mg/3 ml Atropine, 1 mg/10 ml Digoxin, 0.5 mg/2 ml Diltiazem, 25 mg/5 ml Verapamil, 5 mg/2 ml Dopamine, 200 mg/5 ml Epinephrine, 1 mg/10 ml (1:10,000) Epinephrine, 1 mg/1 ml (1:1000) Furosemide, 100 mg/10 ml Heparin, 1000 units/1 ml Isoproterenol, 1 mg/5 ml Labetalol, 40 mg/8 ml Lidocaine, 2 g/10 ml Metoprolol, 5 mg/5 ml Procainamide, 1000 mg/10 ml Nitro-glycerin injection, 50 mg/10 ml Nitro-glycerin tablets, 0.4 mg (bottle) Nitroprusside, 50 mg/2 ml

(continued)

Table 31.3 (continued)

Equipment	Medications
General equipment	
Stethoscope	
Pulse oximeter with multiple site adhesive or reusable sensors	
Blood pressure cuffs (neonatal, infant, child, adult large and small)	
Glucometer with strips	
Alcohol–chlorhexidine hand rub	
Alcohol swabs, alcohol chlorhexidine hand rub	
Micropore 1″	
Elastic tape	
Cotton tape	
Digital thermometer	
Urinary catheter (Foley's) 10, 12, 14, 16	
Urometer and urobag	
Irrigating syringe (60 ml), catheter tip	
Torch, flashlights with extra batteries	
Nasogastric tubes, assorted sizes	
Infant feeding tubes	
Xylocaine jelly	
Spinal immobilization device	
Arm boards (adult and pediatric)	
Soft restraints for upper and lower extremities	
Surgical dressings	
Kelley clamp	
Trauma scissors	
Ointments—soframycin, betadine, neosporine	
Betadine skin prep	
Distilled water 500 ml	
Communications backup (e.g., cellular telephone)	

Table 31.4 A suggested pre-transfer checklist for critically ill patients

Is the patient stable for transport?	Ready for departure?
Airway and breathing Airway safe or secured by intubation/tracheostomy ☐ Tracheal tube position confirmed on chest X-ray ☐ Adequate spontaneous respiration or controlled ventilation established on transport ventilator ☐ ABG parameters confirming adequate gas exchange ☐ Sedated and paralyzed as appropriate ☐	Patient Stable and secured on transport trolley ☐ Appropriately monitored: ECG, BP, SpO_2, Temp, $EtCO_2$ ☐ All infusions running ☐ All lines adequately secured and labeled ☐ Adequately sedated and paralyzed ☐ Adequately wrapped to prevent hypothermia ☐
Circulation Heart rate optimized ☐ BP optimized ☐ Tissue and organ perfusion adequate ☐ Any obvious bleeding controlled ☐ Circulating blood volume restored ☐ Adequate hemoglobin ☐ At least two routes of venous access ☐ Arterial line and central venous access if appropriate ☐	Equipment Appropriately equipped ambulance ☐ Appropriate/checked equipment and drugs ☐ Pre-drawn up, labeled, and capped medication syringes ☐ Batteries checked (spare batteries available) ☐ Sufficient oxygen supplies for anticipated journey ☐ Portable phone charged and available ☐ Money for emergencies ☐
Neurology Raised ICP managed appropriately ☐ Seizures controlled, metabolic causes ruled out/controlled ☐	Staff Transfer risk assessment completed ☐ Staff adequately trained and experienced ☐ Received appropriate handover ☐ Adequately clothed and insured ☐
Trauma Cervical spine stabilized ☐ Pneumothorax drained ☐ Intra-abdominal and intra-thoracic bleeding controlled ☐ Intra-abdominal injuries adequately investigated and managed appropriately ☐ Pelvic/long bone fractures stabilized ☐	Organization Case records, images, lab results, blood collected ☐ Transport documentation prepared ☐ Location of hospital bed and receiving doctor known ☐ Receiving unit advised of departure time and estimated time of arrival ☐ Telephone numbers of referring and receiving units available ☐ Ambulance crew briefed ☐ Relatives informed about everything ☐ Return travel arrangements done ☐
Metabolic Blood glucose ≥ 90 mg/dl ☐ Potassium ≤ 5 mmol/l ☐ Calcium^{++} ≥ 1 mmol/l ☐ Acid–base balance acceptable ☐ Temperature maintained ☐	Pre-departure Patient and trolley secured ☐ Ventilator connected to ambulance oxygen supply ☐ Electrical equipment plugged into ambulance power supply ☐ All equipment safely mounted ☐ Staff seated and wearing seat belts where applicable ☐

Step 6: Monitor Closely During Transport

For critical patients who are being shifted from ICUs, it is desirable to have the same level of monitoring en route. The minimum monitoring should include the following:

- Continuous clinical observation.
- Continuous ECG monitoring.
- Continuous pulse oximetry.
- Invasive BP monitoring is preferred in sick patients, especially on vasoactive medications, and also reduces battery use of the monitor due to intermittent NIBP measurement; otherwise, periodic measurement of blood pressure, pulse rate, respiratory rate, etc.
- Selective patients may benefit from capnography, continuous intra-arterial blood pressure monitoring, and intracranial pressure monitoring.

Step 7: Take Care of Safety During Transport

- Patients should be secured to the transport trolley by means of appropriate restraint (e.g., 5-point harness/straps).
- Pressure areas (including neurovascular bundles) should be appropriately protected.
- Warming/insulating blankets should be used to keep the patient warm unless otherwise contraindicated.
- Indwelling lines and tubes should be secure and visible/accessible.
- All equipment (including transfer bags) must be securely stowed. Equipment should be either fastened to the transport trolley or securely stored in appropriate lockers in the ambulance. When this is not possible, equipment should be placed on the floor against the bulkhead wall. Under no circumstances should equipment (e.g. syringe pump) be left on top of the patient trolley. This may become a dangerous projectile in the event of a sudden deceleration. Gas cylinders must be held in secure housing.
- Staff should remain seated at all times and wear the seat belts provided. Adequately resuscitated and stabilized patients should not normally require any significant changes to treatment during transport. If, however, despite meticulous preparation, unforeseen clinical emergencies arise and the patient requires intervention, this should not be attempted in a moving ambulance. The vehicle should be stopped appropriately in a safe place before administering treatment.
- High-speed journeys should be avoided except where strictly necessary. Blue lights and sirens may be used to aid passage through traffic to deliver a smooth journey.

- During the transport of patients with communicable infectious diseases, the team must follow local and/or international infection control guidelines and use appropriate PPEs.

Step 8: Document and Handover

Effective communication and comprehensive formalized hand-off between transporting and receiving teams is an important issue to enhance safety and should be mandatory.

- Clear records should be maintained at all stages. These should include details of the patient's condition, the reason for transfer, names of referring and accepting consultants, clinical status before transfer, and details of vital signs, clinical events, and therapy given before, during, and after transport.
- On arrival at the receiving hospital, there should be a formal handover between the transport team and the receiving medical and nursing staff who will then assume responsibility for the patient's care.
- Handover should include a verbal and written account of the patient's history, vital signs, therapy, and significant clinical events during transport. X-rays, scans, and other investigation results should be described and handed over to the receiving staff.
- Standardized documentation should be developed across networks and should be used for both interhospital and intrahospital transport. This should include a core data set for audit purposes and the transport team should be able to retain a duplicate for such purposes.

Special Considerations 1: ECMO Transport

ECMO transfer (Table 31.1) is a newer addition to the complexity of critical care transports. Detailed recommendations are outlined in ELSO guidelines while a few important points are mentioned below.

- Mobile ECMO Team: A team leader who can be an experienced ECMO provider and cannulation provider, an ECMO specialist like a trained perfusionist, a nurse or respiratory therapist, and a medical transport person. Cross-training between them with high-fidelity simulation is strongly recommended.
- The mobile ECMO team should be self-sufficient in providing full ECMO care, including all ECMO-related equipment, medications, monitoring, and point-of-care diagnostic devices.
- Pre-prepared, fully stocked, and checked ECMO bag is recommended prior to team mobilization.
- During primary ECMO missions, the patient is to be adequately stabilized post-cannulation and initiation of ECMO prior to transport.

Special Considerations 2: Aeromedical Transport of Critically Ill Patients

The air evacuation team should be familiar with high-altitude physiology, cabin decompression, dysbarism, air expansion in cavities, barotrauma, and other issues that may create problems unique to this mode of travel.

- Staff involved in aeromedical transport must have a high level of expertise, specialist knowledge, and additional practical training in aeromedical transfer.
- Some practical issues that may be relevant for those preparing a patient for air transfer:
  - A fall in barometric pressure results in a reduction in alveolar PAO_2 and may lead to hypoxemia. Increased FiO_2 is mandatory for all aeromedical transfers.
  - At lower atmospheric pO_2 (unpressurized cabins) oxygen can bubble out of the solution, leading to hyper-oxygenation of the ECMO circuit, which must be prevented.
  - A fall in barometric pressure also leads to an increase in the volume of gas-filled cavities within the patient. Endotracheal tube cuff pressure should be monitored or the cuff filled with saline. Pneumothorax must be drained. Nasogastric tubes should be inserted and placed on free drainage. Pneumoperitoneum and intracranial air are relative contraindications to air transport. Tissues may also swell, and plaster casts should be "split."
  - Increased altitude is also associated with a fall in temperature; additional measures may be required to keep the patient warm.
  - Noise and vibration may cause nausea, pain, and motor dysfunction. Anti-emetic pre-medication should be available for patients and transfer personnel and ear protection to be provided.

Suggested Reading

Agizew TB, Ashagrie HE, Kassahun HG, Temesgen MM. Evidence-based guideline on critical patient transport and handover to ICU. Anesthesiol Res Pract. 2021;2021:6618709. https://doi.org/10.1155/2021/6618709.

Australasian College of Emergency Medicine. Australian and New Zealand College of Anaesthetists, College of Intensive Care Medicine of Australia and New Zealand. PS52 Guidel Transp Crit Ill Patients. 2015. Available at: http://www.anzca.edu.au/documents/ps52-2015-guidelines-for-transport-ofcritically-i.pdf.

Labib A, Erin A, Cara A, et al. Extracorporeal life support organization guideline for transport and retrieval of adult and pediatric patients with ECMO support. ASAIO J. 2022;68(4):447–55. https://doi.org/10.1097/MAT.0000000000001653.

The faculty of intensive care medicine. Intensive Care Society. Guidance on: The transfer of the critically ill adult. Available from: https://www.ficm.ac.uk/sites/ficm/files/documents/2021-10/Transfer_of_Critically_Ill_Adult.pdf.

Chest Imaging in the ICU

32

Anirban Hom Choudhuri, Priyanka Harisinghani Chhabra,
and Bhuvna Ahuja

Case Vignette

A 58-year-old female presented to the emergency department with fever, chills, and sudden worsening of dyspnea for the past three days. The patient had a history of asthma and is a known case of rheumatoid arthritis on chronic prednisolone therapy (10 mg/day) and methotrexate. On examination, the patient had tachycardia, tachypnoea, and the use of accessory muscles for respiration. Which imaging modality will you recommend to further investigate this patient?

Chest imaging is perhaps the most commonly performed diagnostic imaging in intensive care units (ICUs) worldwide. Selecting an appropriate modality of chest imaging helps in establishing the diagnosis, evaluating the progression of the disease, and helping in prognosticating outcomes. Although chest radiography (CXR) is one of the simplest examinations in ICUs, other newer modalities like ultrasound, computerized tomography (CT), and nuclear scanning techniques are also emerging.

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Step 1: Understand and Utilize Various Imaging Modalities

Normal Chest X-Ray in the ICU

- Chest radiography in the intensive care unit (ICU) typically involves an anteroposterior (AP) projection rather than the standard posteroanterior (PA) view (Figs. 32.1 and 32.2).
- Optimal image acquisition requires a 72-inch patient-to-image receptor distance in the upright position at full inspiration. However, due to patient immobility, AP radiographs are often obtained at a shorter distance (40 inches) in the supine or sitting position. This suboptimal technique results in mediastinal and cardiac magnification caused by gravitational and geometric factors.

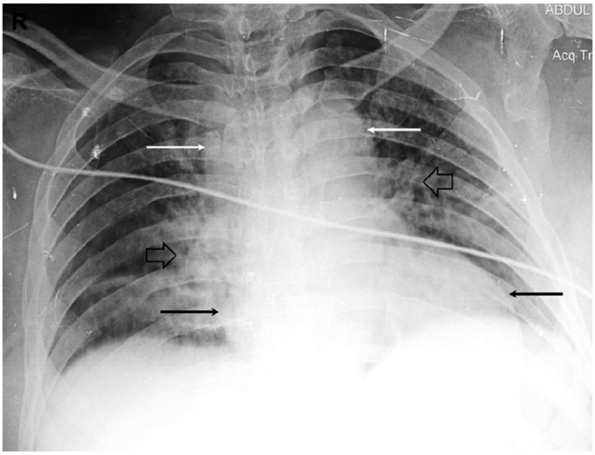

Fig. 32.1 Chest radiograph frontal view in supine AP position showing no sign of volume gain or volume loss. Rotation is a common feature in critical care supine radiographs due to which the left hemithorax shows slightly increased density than the right; this should not be mistaken for a pathology

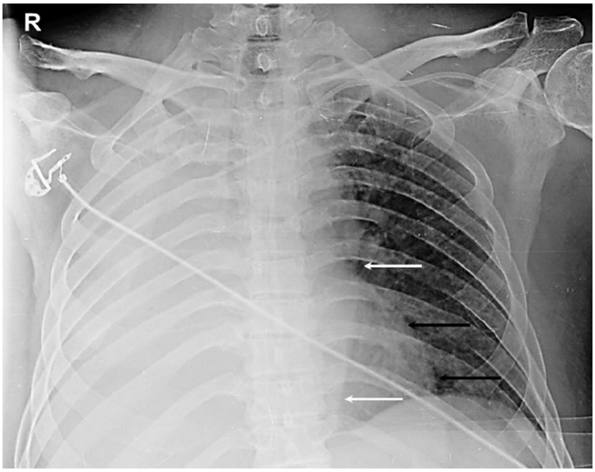

Fig. 32.2 Chest radiograph frontal view in erect AP position showing complete "whiteout" of the right hemithorax. The right cardio-mediastinal silhouette and the right hemidiaphragm outline are not visualized (D.D.: pneumonia, lung collapse, and pleural effusion)

- Additionally, the supine position alters pulmonary vascular physiology, leading to blood redistribution to lung apices, which is a normal finding in this context but may be misinterpreted as a pathology on a PA radiograph.
- Other limitations of supine radiographs include difficulty in differentiating pleural effusions from airspace disease and detecting pneumothorax. Obtaining a fully inspired radiograph in ICU patients is challenging due to patient cooperation and pain issues.

Step 2: Identifying Tubes and Lines and Other Devices

Tubes, lines, and drainage catheters are critical components in the management of critically ill patients. Accurate placement and ongoing monitoring of these devices are essential for optimal patient care. The initial portable chest radiograph is indispensable for verifying correct positioning and identifying potential complications. Table 32.1 gives the correct positioning of various lines and tubes seen on a chest radiograph.

Table 32.1 Identifying lines and tubes and other devices

Endotracheal tubes (Fig. 32.3)	Safe level 5 cm from carina (T4–T5 interspace), minimum distance 2 cm
Nasogastric tube	Tip anywhere in the stomach (≥10 cm) distal to the gastro-esophageal junction, hence seen below the left hemidiaphragm (unless situs inversus); point downward toward the midline; no radio-opaque tip Ideally the distal duodenum (Fig. 32.7)
CVP line (Figs. 32.4 and 32.5)	The tip should be at the cavo-atrial junction usually located at the first anterior intercostal space toward the right of the sternal margin. In most patients, cavo-atrial angle may be seen in the right mediastinal silhouette (viz. straight line of vena cava and outward bulge of right atrium). Ideally placed between proximal venous valves of the subclavian or jugular veins and the right atrium.
Thoracostomy tube (Fig. 32.6)	The position of the last side hole in a thoracostomy tube can be identified by an interruption in the radiopaque line. This interruption in the radiopaque line should lie within the thoracic cavity, if not and or with evidence of subcutaneous air, a misplaced tube is suspected. Incorrectly placed tubes for empyemas may delay drainage and result in the loculation of the purulent fluid. Thoracostomy tubes placed within pleural fissures often cease to drain when the lung surfaces become apposed.
Cardiac pacemakers	The tip of the cardiac pacemaker should be at the apex of the heart, and there should be no sharp angulations along the length of the pacemaker wires. The lateral radiograph should show the tip embedded within the cardiac trabeculae. For correct placement to have occurred, the tip should appear 3–4 mm beneath the epicardial fat pad. A tip that appears to be placed beyond the epicardial fat stripe may have perforated the myocardium. Cardiac pacers placed within the coronary sinus appear to be directed posteriorly on the lateral chest radiographs.

(continued)

Table 32.1 (continued)

Intercostal drain (ICD)	Tip should be evaluated on two views (AP and lateral). Unless placed in a loculated effusion (when it is located at the effusion site), it should point upward and located at a posterior or lateral costophrenic angle.
Pericardial drain	Tip on the left of the midline into the pericardial space. A lateral view may also be needed to confirm.
Intra-aortic balloon pump (IABP)	Tip at the level of the aortopulmonary window. A lateral view may also be needed to confirm.

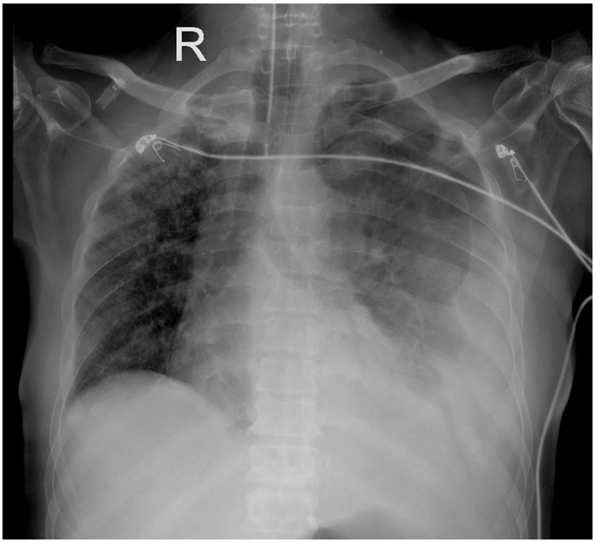

Fig. 32.3 Chest X-ray AP view showing the position of endotracheal tube and left sided pleural effusion

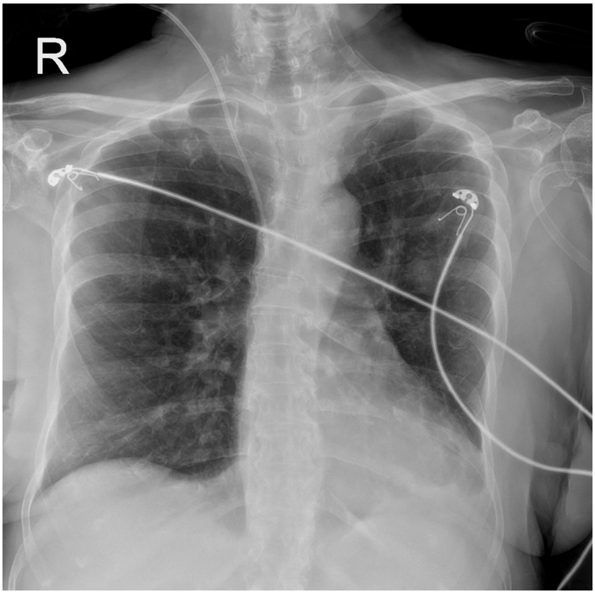

Fig. 32.4 Chest X-ray AP view showing the position of the internal jugler line

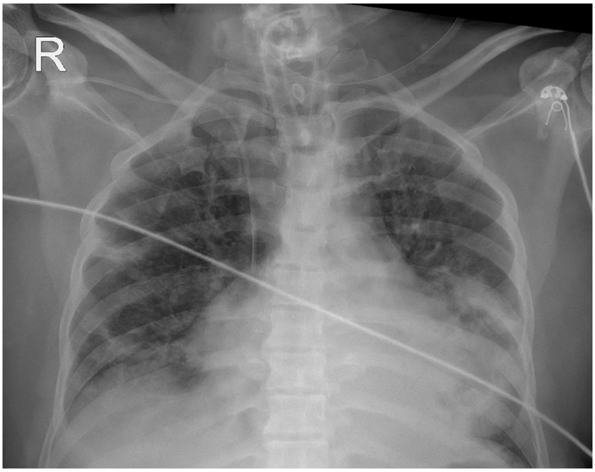

Fig. 32.5 Chest X-ray AP view showing the position of the subclavian central line

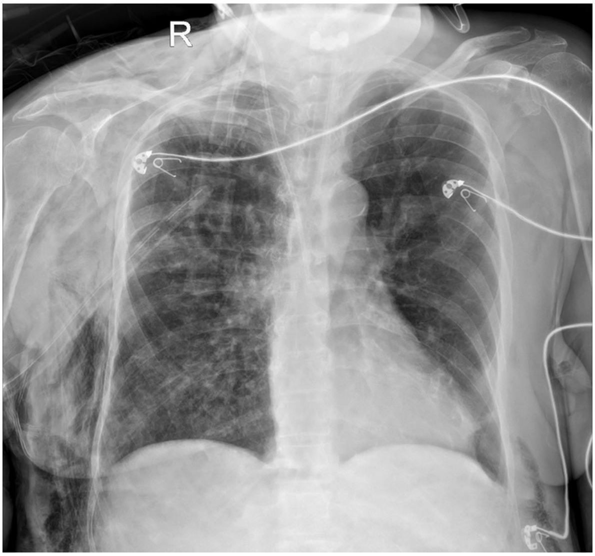

Fig. 32.6 Chest X-ray AP showing subcutaneous emphysema and intercostal tube

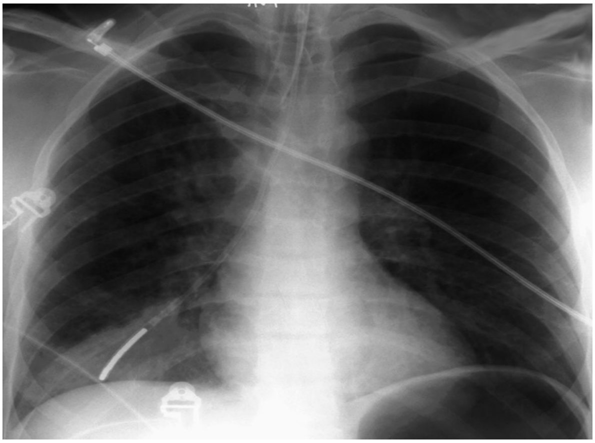

Fig. 32.7 Chest X-ray AP view showing a nasogastric tube in the lung

Common Conditions on Chest X-Ray

Pleural Effusion

- Pleural effusion, an accumulation of fluid within the pleural cavity, is a common clinical finding, particularly in critically ill patients (Fig. 32.3).
- Its etiology is diverse, encompassing conditions such as congestive heart failure, nephrotic syndrome, pneumonia, pulmonary embolism, and malignancy. The fluid's characteristics—transudative or exudative—offer valuable diagnostic clues.

Pericardial Effusion

- Pericardial effusion, characterized by fluid accumulation within the pericardial sac, is often asymptomatic unless it develops rapidly, leading to cardiac tamponade.
- Its causes range from viral infections and autoimmune diseases to malignancy and trauma.
- Radiographic detection of pericardial effusions is challenging due to their subtle manifestations. In some cases, a globular or "water bottle" cardiac silhouette may be observed.

Atelectasis

- Atelectasis is a condition characterized by the collapse or incomplete expansion of lung tissue.
- Radiographically, it manifests with a constellation of findings: elevation of the ipsilateral hemidiaphragm, displacement, and crowding of pulmonary vasculature, compensatory hyperinflation of the unaffected lung with resultant splaying of vessels, mediastinal shift toward the affected side, and obscuration of normal lung contours (silhouetting).

Aspiration

- Aspiration pneumonitis is characterized by pulmonary consolidation that typically emerges within the first 48 h. These consolidative opacities are often bilateral and perihilar but may display asymmetric distribution.
- Improvement in the consolidative process usually begins by the third day, although complications such as lung abscess or pleural effusion can prolong the course and worsen the radiographic findings.

Pulmonary Embolism

- Chest radiographic findings are generally nonspecific. In the absence of pulmonary infarction, subtle radiographic signs may emerge, including discoid atelectasis, elevated diaphragms, an enlarged pulmonary artery (Palla's sign), and diminished blood flow distal to the occlusion (Westermark's sign).
- The complications of pulmonary infarction, such as multifocal consolidation, pleural effusions, and the distinctive Hampton's hump, can further complicate the radiographic interpretation.

Pneumonia in the ICU (Fig. 32.8)

- Chest imaging assumes a pivotal role in diagnostic confirmation. However, differentiating pneumonia from other airspace opacities, such as atelectasis and acute respiratory distress syndrome (ARDS), can be challenging.
- Pneumonia typically manifests radiographically as patchy consolidation or ill-defined nodules, often exhibiting a bilateral distribution and predilection for gravity-dependent lung regions.
- In certain cases, a symmetric pattern mimicking pulmonary edema can arise, particularly with specific causative organisms, resulting in rapid and extensive

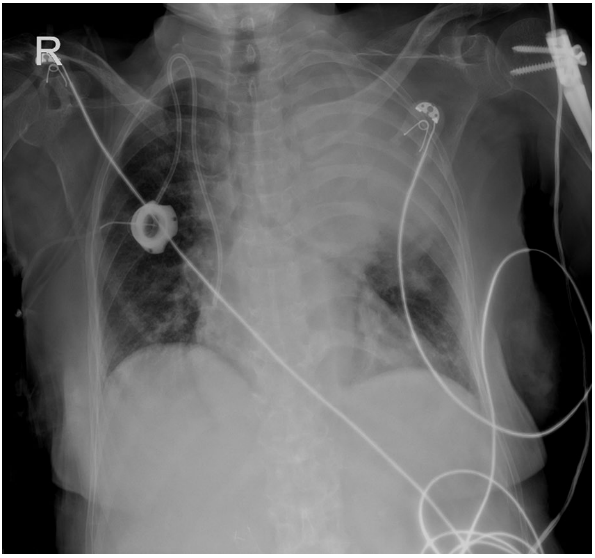

Fig. 32.8 CXR showing left upper lobe consolidation

lung involvement. The presence of patchy consolidation, segmental involvement, air bronchograms, and associated pleural effusions lends support to the diagnosis of pneumonia.

- It is crucial to recognize that pleural effusions secondary to Gram-negative organisms are more likely to represent empyema, necessitating drainage procedures.
- Moreover, pneumonia in the ICU can lead to severe complications, including abscess formation and bronchopleural fistulas. Apart from common conditions, cardiac pacemakers can also be seen on chest radiographs.

Pneumothorax

Pneumothorax is defined as the accumulation of air within the pleural space. Its etiology is varied, encompassing spontaneous, traumatic, and disease-related occurrences. The characteristic radiographic appearance is influenced by patient positioning. Supine radiographs are characterized by "deep sulcus sign" (increased radiolucency at the costophrenic sulcus due to anterolateral air accumulation). Visualization of the diaphragm's superior surface and the proximal inferior vena cava further supports this diagnosis (Figs. 32.9 and 32.10). Subcutaneous emphysema can be seen on chest X-rays (Fig. 32.6).

Pulmonary Edema in the ICU

This is very commonly seen in the ICU (Fig. 32.11) with characteristic parahilar shadows and pleural effusion.

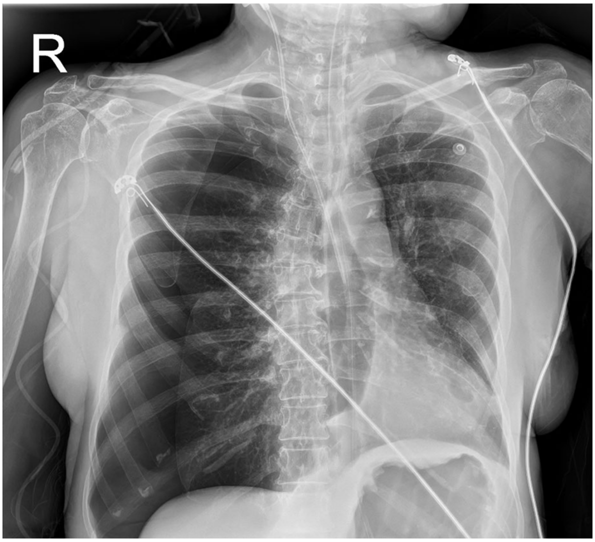

Fig. 32.9 Chest X-ray AP view showing tension pneumothorax. Patient was hemodynamically unstable

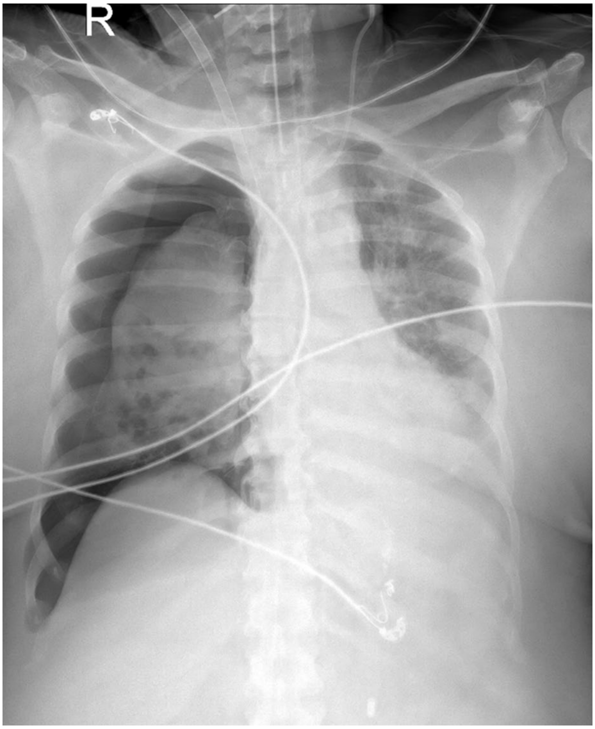

Fig. 32.10 Chest X-ray showing pneumothorax with deep sulcus sign

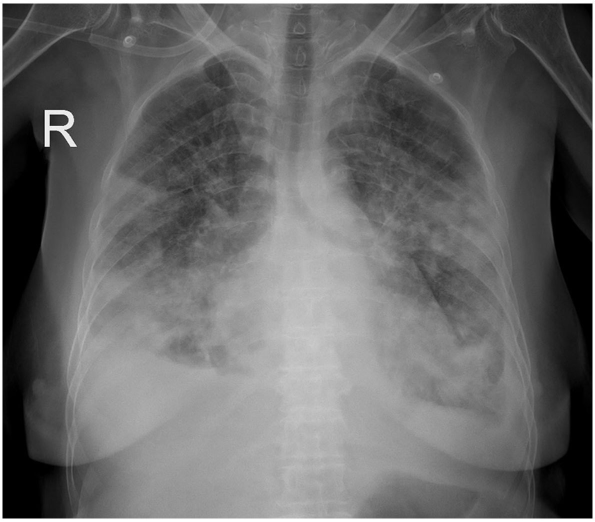

Fig. 32.11 Chest X-ray AP view showing pulmonary edema

Step 3: Utilizing Ultrasonography

- Ultrasonography (USG) of the lungs is easy, noninvasive, free of radiation, and available at the bedside. As compared to chest radiography, lung USG is more sensitive and has similar specificity in diagnosing common chest conditions like pneumothorax, pleural effusion, consolidation, and pulmonary edema.
- This is the reason why USG has become an extremely popular diagnostic modality in recent times. Lung ultrasound in critically ill patients (LUCI) is an exception as it is artifact-based as compared to other modalities that visualize the target organ directly.

Patient Position The patient can be placed in a sitting, supine position, or lateral decubitus position.

USG Machine and Ergonomics One can use either low-frequency, curvilinear probe or high-frequency, linear probe. It is desirable to place the probe on a long axis, perpendicular to the skin surface. Care should be taken not to place the probe over ribs as it creates acoustic shadowing.

Areas of Interest Merlin's space is defined as the area between the pleural line on one side and the bottom of the screen on the other side. As per the BLUE (bedside lung ultrasound in emergency) protocol, lungs are divided into three sites for examination. Both hands are placed on the patient's chest.

1. The upper BLUE point lies in the middle of the upper hand.
2. The lower BLUE point lies at the center of the lower hand.
3. PLAPS (posterior lateral alveolar pleural syndrome) point—Tracing the lower BLUE point posteriorly at the point where it meets the posterior axillary line lies the PLAPS point. This is the best point for visualizing pleural effusion and consolidation.

Lung Ultrasound Several lung signs arise as artifacts in lung USG. They are as under:

- A-lines: A-lines represent air space and are a result of reverberation artifact of the pleural line. They are also found abundantly in patients with pneumothorax. Figure 32.12 shows A-lines.
- Normal respiration moves both the layers of the pleura. This is referred to as the lung sliding sign. This normal lung sliding gets impaired when there is a collection of either air (pneumothorax) or fluids (pleural effusion) in the pleural space

Pulmonary edema The presence of B-lines signify interstitial or interalveolar edema (Fig. 32.13). B-lines (>3 mm) are hyperechoic, vertical lung rockets arising

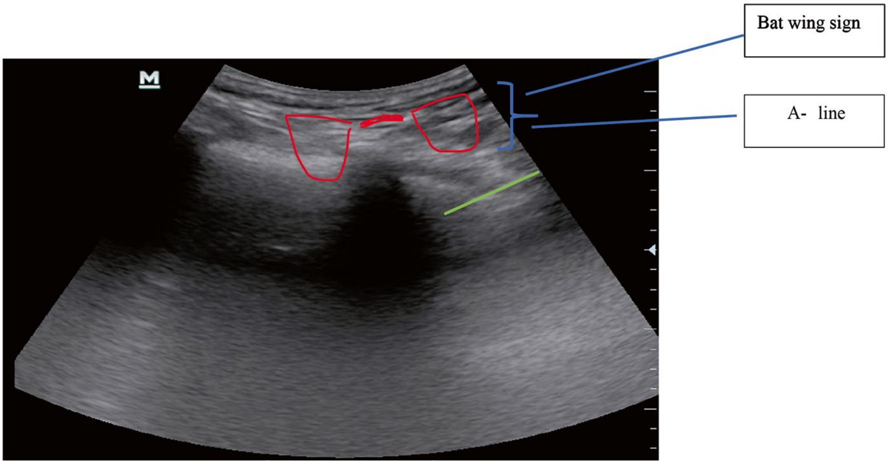

Fig. 32.12 Batwing sign. The pleural line appears as the body of the bat, while the ribs resemble the wings of the bat. Normal lungs: The pleural line with adjacent ribs creates the characteristic batwing sign

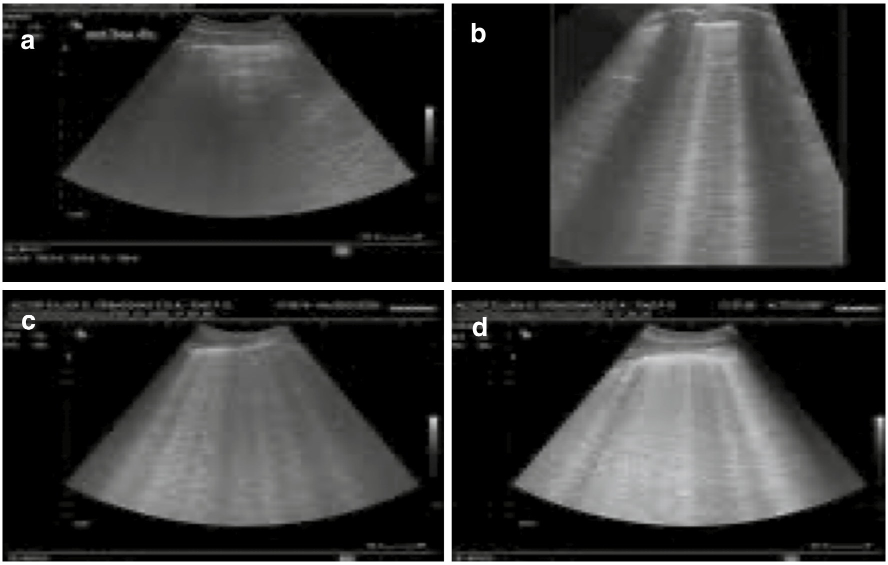

Fig. 32.13 B-lines seen on lung ultrasound

from the pleural line, extending till the end of the screen and moving with respiration. The presence of B-lines obscures A-lines.

Pneumothorax Normal lungs appear as sea shore on M-mode USG, known as seashore sign (Fig. 32.14). The presence of air in pleural space obscures normal sea

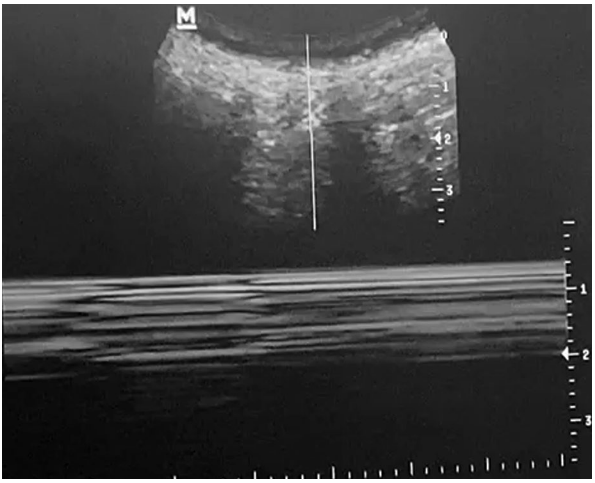

Fig. 32.14 Barcode sign—Pneumothorax on lung ultrasound seen as barcode sign on M-mode

shore signs and produces a barcode-like image on an M-Mode known as a barcode or stratosphere sign. Careful ultrasound examination reveals a point where the sea shore sign meets the barcode sign, known as lung point. The presence of lung point is almost 100% specific and is pathognomic for pneumothorax.

Pleural Effusion Accumulation of fluid in the pleural space leads to the separation of visceral and parietal layers of the pleura and the collapse of surrounding lung tissue. This together with normal up and down movement of the diaphragm during normal respiration appears as a curtain sign.

The separated parietal and visceral layers together with adjoining ribs give the appearance of a quadrilateral (figure with four sides) known as a quad sign. The compressed lung is visualized under ultrasound as jellyfish (Fig. 32.15).

Consolidation or Pneumonia Subpleural consolidations produce irregular lines with hyperechoic underlying lung, known as shred sign or fractal sign (Fig. 32.16).

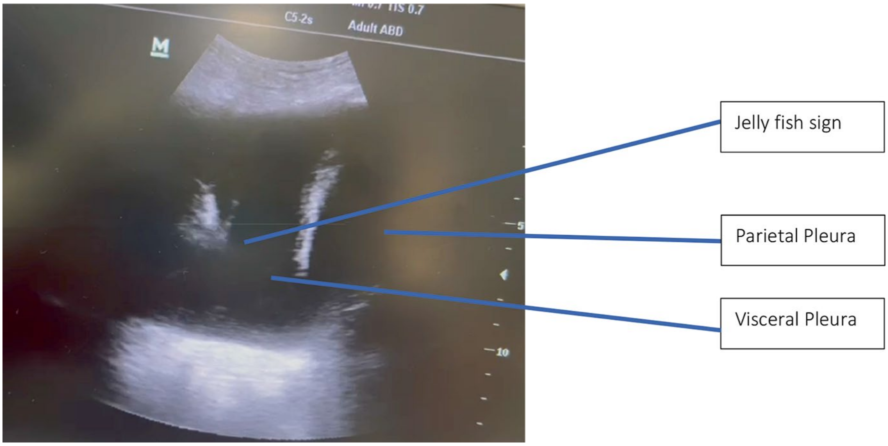
TIS 0.7
C5-2s
Adult ABD
M
5
10
Jelly fish sign
Parietal Pleura
Visceral Pleura

Fig. 32.15 Jellyfish sign—Pleural effusion is seen as a separation of two layers of pleura with a compressed adjacent lung giving the appearance of jellyfish

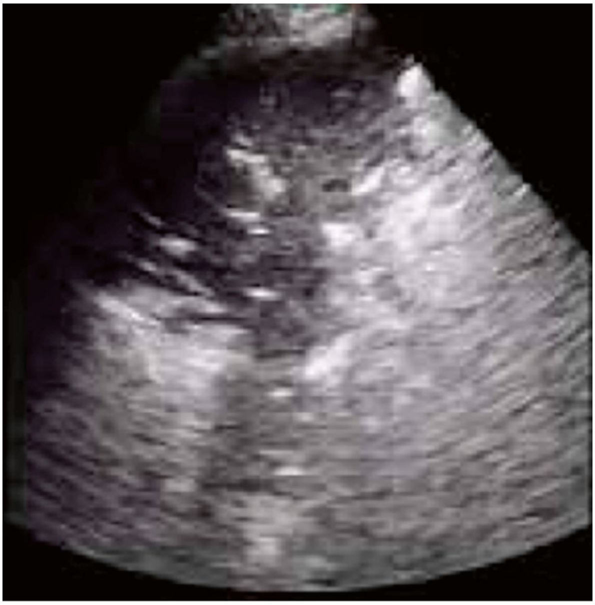

Fig. 32.16 Shred sign—Subpleural consolidations appear as shreds of pleural line known as shred sign

Step 4: Role of Computerized Tomography (CT) Scan of Chest in Diagnosing Chest Disorders

- Computerized tomography (CT) scans are more sensitive in identifying small pathology of the thorax, which might get missed on chest radiographs.
- CT scan is based on taking several cross-section images of the chest and thorax from different rotational angles and then, making a digital reconstruction of the three-dimensional image.
- The amount of radiation removed while passing through tissue in cross-section is termed a Hounsfield Unit (HO).
- Tissues removing more radiation are given positive HU like muscle and bone. Water has zero, and lungs and fat are given negative HU values (Table 32.2).
- The use of thin collimation sections, preferably 1–2 mm, improves the spatial resolution of images. This combined with high-frequency digital reconstruction of images improves image quality and is termed a high-resolution CT (HRCT) scan. With the advent of modern multi-slice spiral CT machines, the image quality of NCCT is comparable except that post-processing is done with a specific software in HRCT.

Table 32.2 Appearance of various structures on the basis of density

Substance	Density (HU)	Appearance on CT scan
Air	−1000	■
Fat	−50	■
Water	0	■
Soft tissue	+30 to +60	▒
Bone	+1000	□

Contrast-Enhanced Computerized Tomography (CECT) Thorax

- Administration of contrast accentuates the vascular structures and helps in better delineation of vascular from nonvascular structures. A good vascular access should always be secured, preferably 18 G intravenous (i.v.) cannula in the antecubital vein with adequate injection pressure (3–6 ml/s).
- A delay of 55–70 s is advisable to allow vascular structures for enhancement. CECT chest is useful in the evaluation of hilar structures, mediastinal structures, pleural diseases, lobar collapse, aortic dissection, and pulmonary embolism.

Computerized Tomography Pulmonary Angiography (CTPA)

CTPA helps evaluate pulmonary artery and for evaluation of a patient with suspected pulmonary embolism. CTPA is either performed with the patient breathing freely or preferably with a shallow inspiratory hold to avoid dilution with blood coming from the inferior vena cava.

Step 5: Approach for Interpretation of HRCT Chest

- A thorough understanding of lung anatomy is required for the interpretation of a CT scan of the chest.
- The secondary lobule is the basic anatomical and functional unit of the lung.
- The secondary lobule is the smallest lung unit, composed of up to 30 acini, each cluster having its own pulmonary artery and terminal bronchiole. In between secondary lobules are the septae, which are composed of connective tissue, distal pulmonary veins, and lymphatics.
- Peripheral lobules are cuboidal whereas central ones are hexagonal in shape. Interpretation of lung parenchymal disease depends primarily on the pattern of involvement of secondary lobule.

Centrilobular involvement Centrilobular area is the central part of the secondary lobule. Centrilobular areas are usually affected by disorders that enter the lungs through the airways. These diseases begin from the center of the secondary lobule and spread toward the peripheral part like emphysema, bronchiolitis, hypersensitivity pneumonitis, etc.

Peri-lymphatic involvement Peri-lymphatic areas are usually affected in diseases that spread via bloodstream or lymphatics like carcinoma, sarcoidosis, pulmonary edema, etc., and primarily affect the peripheral part.

Other Patterns of Involvement Diseases can cause various patterns on CT scan of the chest like reticular (fine line-like), nodular (in the form of small nodes), high density (more radio-opaque), or low density (less radio-opaque).

1. *Reticular pattern*—Thickening of interlobular septa and interstitial fibrosis leads to several fine linear opacities within a secondary pulmonary lobule. This pattern is characteristic of idiopathic pulmonary fibrosis. It appears on a CT scan as a network of interlacing patterns producing a mesh-like appearance. Small cystic spaces lined by alveolar epithelium give the appearance of *honeycombing*.
2. *Nodular pattern*—Presence of several nodules on CT film indicates the presence of a predominant nodular pattern of lung involvement. Based on the location of nodules in relation to the secondary lobule, they are classified into three categories: centrilobular, peri-lymphatic, and random (Fig. 32.17).
   (a) *Centrilobular* nodules are situated on the center of the secondary lobule and spare the pleural surfaces, e.g., bronchiolitis, hypersensitivity pneumonitis, etc.
   (b) *Peri-lymphatic* nodules are situated on either pleural surfaces or in interlobular septa, e.g., sarcoidosis, silicosis, etc.
   (c) *Random* distribution of nodules like tuberculosis and metastasis, where nodules are distributed randomly on pleural surfaces and in centrilobular areas. Fig. 32.18 shows a basic interpretation of the HRCT chest based on the pattern of involvement of the secondary lobule.
3. *High attenuation (ground glass opacity)*: When a diffuse increase in lung attenuation does not obscure underlying vessels, known as ground glass opacity (GGO), and in case it obscures underlying vessels, known as consolidation.

This pattern could be obtained whether airspaces are filled with pus, edema, inflammation, or due to the involvement of the lung interstitium with fibrosis. GGOs are a nonspecific finding on HRCT chest, and their presence should always correlate with other CT findings. A crazy pavy pattern occurs when ground glass opacities are combined with septal thickening. This pattern is seen in alveolar proteinosis, sarcoidosis, neoplasm, etc.

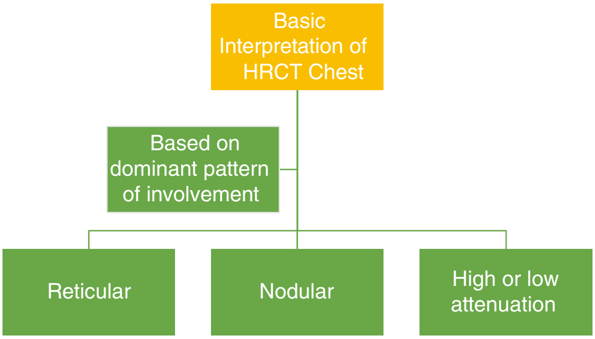
Basic Interpretation of HRCT Chest
Based on dominant pattern of involvement
Reticular
Nodular
High or low attenuation

Fig. 32.17 Basic interpretation of HRCT chest on the basis of the dominant pattern of involvement *HRCT* high-resolution computerized tomography

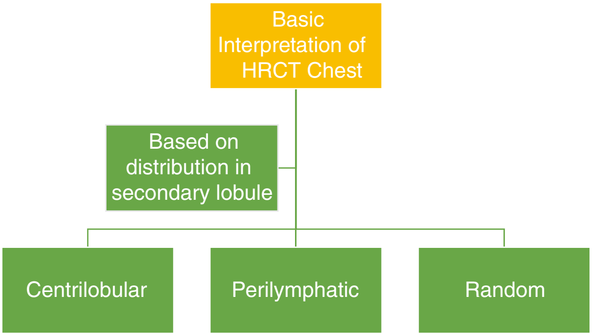
Basic Interpretation of HRCT Chest
Based on distribution in secondary lobule
Centrilobular
Perilymphatic
Random

Fig. 32.18 Basic interpretation of HRCT chest on the basis of distribution in secondary lobule *HRCT* high-resolution computerized tomography

Low Attenuation Diseases that lead to air trapping in the lungs lead to characteristic low attenuation patterns, e.g., emphysema, lung cysts, bronchiectasis, etc.

A few respiratory diseases with characteristic findings on HRCT chest are listed below:

A. *Asthma*

   CT chest is an extremely useful tool in the identification of the cause of acute decompensation of an asthmatic patient. Pneumothorax and pneumomediastinum are easily diagnosed with the help of a CT scan. Other HRCT findings include bronchial wall thickening, air trapping in expiratory films, narrowing of the bronchial lumen, and bronchiectasis in up to 60% of cases.

B. *Bronchiectasis*

   Bronchiectasis is characterized by dilation of central bronchi with a lack of peripheral tapering. Often, there is an accumulation of mucus in the bronchial lumen.

C. *Allergic Bronchopulmonary Aspergillosis (ABPA)*

   ABPA is a lung disease occurring in patients with asthma due to hypersensitivity reaction to *Aspergillus fumigatus*. HRCT films typically show central bronchiectasis with extensive mucoid impaction and atelectasis.

Suggested Reading

Verma A, Ahuja B, Duggal S, Kumar I. Respiratory system, imaging in radiology, 2023; 1–27.

Khan AN, Al-Jahdali H, Al-Ghanem S, Gouda A. Reading chest radiographs in the critically ill (Part I): normal chest radiographic appearance, instrumentation and complications from instrumentation. Ann Thorac Med. 2009a;4(2):75–87.

Khan AN, Al-Jahdali H, Al-Ghanem S, Gouda A. Reading chest radiographs in the critically ill (Part II): Radiography of lung pathologies common in the ICU patient. Ann Thorac Med. 2009b;4(3):149–57.

Lichtenstein DA, Mezière GA. Relevance of lung ultrasound in the diagnosis of acute respiratory failure: the BLUE protocol. Chest. 2008;134:117–25.

Bhoil R, Ahluwalia A, Chopra R, Surya M, Bhoil S. Signs and lines in lung ultrasound. J Ultrason. 2021;21(86):e225–33. https://doi.org/10.15557/JoU.2021.0036. Epub 2021 Sep 9. PMID: 34540277; PMCID: PMC8439137

Sajjad Z. Understanding HRCT of the lungs. J Coll Physicians Surg Pak. 2008;18(6):327–8.

Ultrasound in the ICU

33

Swarup Shankar Padhi, Shrikanth Srinivasan,
and Deepak Govil

A 50-year-old male, a known case of COPD, presented to the emergency with complaints of shortness of breath and cold clammy extremities. On examination, he was found to be tachypneic, tachycardiac, and hypotensive. A decrease in urine output was also noted. How would ultrasound help in the evaluation and management of this patient?

Ultrasonography is now considered the stethoscope of the intensivist and has become an essential component in evaluating and clinically managing patients admitted to the intensive care unit. Routinely using ultrasound in the ICU can rule out various disorders of the lungs, heart, abdomen, and vasculature and help manage fluid balance, which is an integral component of the ICU. Repeatability, reproducibility, portability, good-quality imaging, and the lack of hazards from radiation make ultrasound a handy tool to dynamically evaluate the various pathological conditions in real time.

Step 1: Understand Thoracic Ultrasound

Air produces artifacts and taking that as an advantage various abnormalities can be diagnosed with good sensitivity and specificity.

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Pleural Line

- With the transducer held in a longitudinal orientation to the skin surface and centered over an intercostal space, a horizontally orientated hyperechoic artefactual line approximately 0.5 cm deep to the origin of the rib shadows is seen, which represents the interface of the visceral and parietal pleural surfaces and is called the pleural line.

Lung Sliding

- During respiration, the two pleural surfaces slide against each other, and this appears as a shimmering white line artifact that moves in synchrony with the respiratory cycle called lung sliding and is identified in B-mode.
- On M-mode ultrasound, lung sliding appears as what is known as the seashore sign, which is characterized by a horizontal linear pattern corresponding to the chest wall, the pleural line appearing like bright granularity and a homogeneous granular pattern, an artifact generated by respiratory cycles and air movement below the pleural line (Fig. 33.1).
- Lung sliding is found in normal lungs and is reduced or absent in various pathologies that affect lung mobility.
- Lung sliding becomes restricted in acute respiratory distress syndrome, chronic adherences, fibrotic lung disease, phrenic palsy, and high-frequency jet ventilation while it is absent in pneumothorax, complete atelectasis, pleural fibrosis, and apnea.

A-Lines

- The normal lung parenchyma cannot be seen beyond the pleural line, as the presence of air prevents penetration of ultrasound waves. When ultrasound beams encounter the air tissue interface, there is a production of artifacts known as

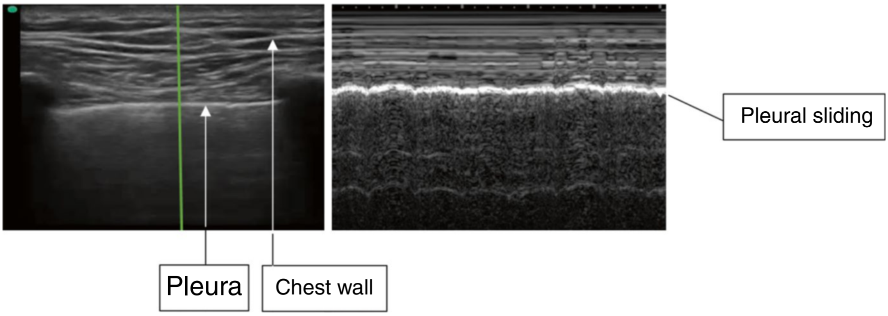


Fig. 33.1 Lung sliding and seashore sign

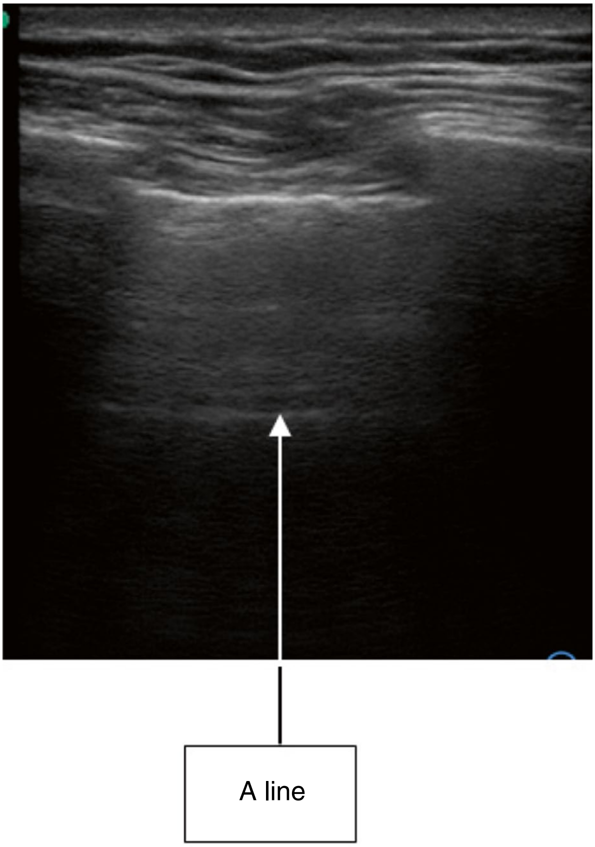


Fig. 33.2 A-lines

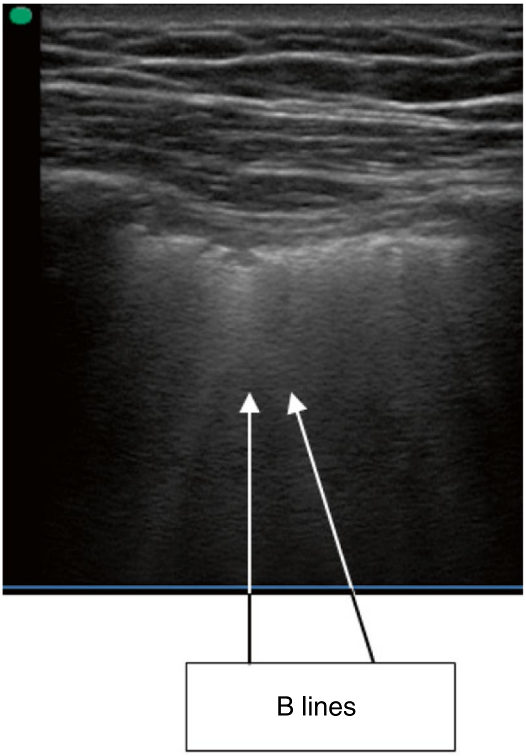
A-lines, which are horizontally orientated lines seen deep into the pleural line (Fig. 33.2). They represent reverberation artifacts from ultrasound reflection between the pleural surface and the chest wall.

- A-lines with lung sliding are consistent with a normal aeration pattern. A-lines with no lung sliding could denote a pneumothorax.

B-Lines

- B-lines are artifacts that appear as vertically orientated laser-like lines extending from the pleural interface to the bottom of the screen without fading and effacing A-lines where the two intersect and they generally move synchronously with lung sliding (Fig. 33.3).
- B-lines strongly correlate with interstitial edema and are formed when air and water are simultaneously hit by ultrasound beams (Fig. 33.3).
- Three or more B-lines in two adjacent intercostal spaces may be considered as significant findings.

Fig. 33.3 B-lines



- Diffuse B-lines in lung parenchyma with a distance of <3 mm are also called lung rockets corresponding with a ground-glass pattern in chest computed tomography scans.
- Since B-lines arise from the pleural line, their presence rules out a pneumothorax in that field.

E-Lines

- E-lines are formed due to subcutaneous emphysema. As the air bubbles infiltrate into the subcutaneous tissues, the tissue air interface moves up from the pleural line to the subcutaneous fat and muscle planes. This leads to the formation of vertical artifacts similar to B-lines but emerging at different levels from the subcutaneous tissues and muscle planes (Fig. 33.4).

Pleural Effusion (Fig. 33.5)

- Using the curvilinear probe (2–5 MHz), a proper evaluation of pleural effusion requires identifying three key findings:

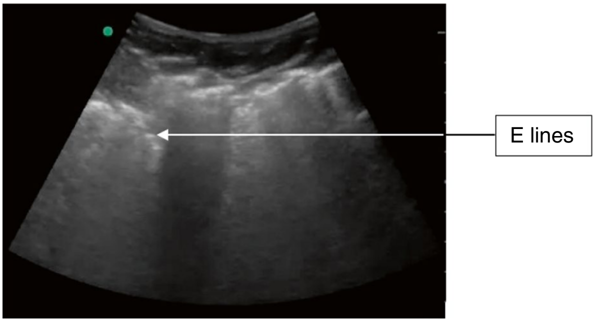


Fig. 33.4 Subcutaneous emphysema

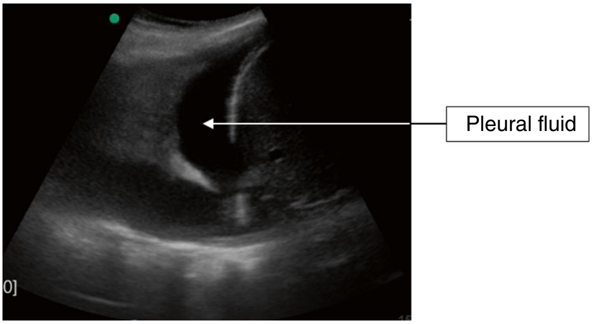


Fig. 33.5 Pleural effusion

  1. Anatomical boundaries: chest wall, lung, diaphragm, and adjacent solid organs (liver/spleen), confirming the intrathoracic location of the collection, especially if a thoracentesis has been planned
  2. Anechoic space: the pleural effusion itself
  3. Dynamic changes: intermittent lung aeration, compressed lung, or both (atelectasis)
- Two signs are associated with pleural effusion:
  1. *Quad sign*: A quadrilateral formed by the chest wall (parietal pleura) above and the pleural line (visceral pleura) below along with the shadow of two adjacent ribs; the intervening space is hypoechoic, which indicates pleural effusion.
  2. *Sinusoid sign*: It's a dynamic sign on M mode wherein the sinusoidal movement of the freely floating lung with each inspiration denotes the presence of an effusion.
- A 15-mm distance is considered the minimum required for safe diagnostic or therapeutic puncture for pleural effusion.

Atelectasis

- The pleural line may move in synchrony with cardiac pulsation in addition to lung sliding that occurs synchronously with the respiratory cycle. This movement, termed lung pulse, is caused by the force of the cardiac pulsation being transmitted to the lung and the visceral pleura. The *lung pulse* is useful for immediate diagnosis of an atelectasis, which is seen as a marked reduction in sliding with pulsation transmitted from the heart.

- The presence of lung pulse also rules out a pneumothorax in that field because it is produced when the two layers of pleura are opposed to each other allowing the transmitted cardiac pulsations to be visualized.
- Absence of dynamic air bronchograms (see below).
- Loss of lung volume and raised hemi diaphragm on the affected side.

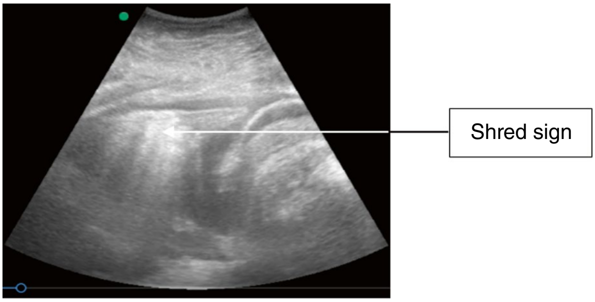
Consolidation

- Consolidations can be either non-translobar or translobar.
- *Shred sign* (Fig. 33.6) indicates non-translobar consolidations, where the border between consolidated and aerated lung appears as an irregular line, known as the fractal line.
- *Tissue-like sign* is used for translobar consolidations, where the lung appears similar to the liver.
- Dynamic air bronchogram: Seen as air artifacts appearing and disappearing with each inspiration and expiration, respectively, within a deaerated or tissue-like hepatized lung. This denotes the patency of the bronchi and bronchioles, while the alveoli are flooded and deaerated. The presence of this sign distinguishes consolidation from atelectasis.

Interstitial Syndrome

- B-line is a comet-tail artifact arising from the pleural line and moves synchronously along with lung-sliding.
- The presence of B-lines 7 mm apart suggests interstitial edema.
- As the number of B-lines increases and becomes confluent (3 mm) apart, it represents alveolar edema.

Fig. 33.6 Shred sign



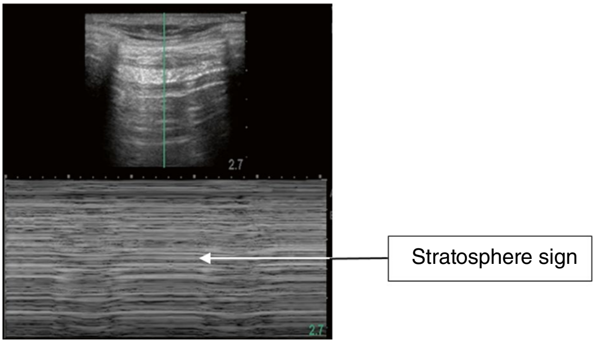


Fig. 33.7 Pneumothorax on M mode: Stratosphere sign

Pneumothorax (Fig. 33.7)

- Absent lung-sliding: The visceral pleura doesn't move against the parietal pleura with respiration using real-time ultrasound assessment.
- *Lung point*: A pathognomonic sign indicating the junction between the sliding and the nonsliding lung. M-mode shows the *stratosphere sign*, characterized by laminar and horizontal artifacts seen below and above the pleural line. This is also known as a Barcode sign.

Airway

- The passage of the endotracheal tube in the trachea can be visualized in real time during intubation by placing the linear probe on the trachea during intubation. Bilateral ventilation is confirmed by visualizing bilateral lung sliding.

Diaphragm

- Diaphragm function can be assessed by estimation of diaphragmatic excursion and thickening fraction, mainly in ventilated patients to assess for weaning. Diaphragmatic excursion is conducted in M mode by using the 12–5 MHz probe towards the dome of the diaphragm. An excursion of <11 mm might indicate failure to successfully extubate. Diaphragm thickening fraction is seen at the point of apposition in the costophrenic angle (7th–9th intercostal space, mid-axillary line) wherein the diaphragm is visualized as a three-layered structure that thickens with every inspiration and thins out in exhalation, the fraction of thickening (inspiratory thickness-expiratory thickness/expiratory thickness × 100) being proportionate to the strength of diaphragmatic contraction. A fraction more than 30% is suggestive of good diaphragmatic strength and less than 15% poor function and could contribute to weaning failure.

BLUE-protocol (Fig. 33.8) (bedside lung ultrasound in emergency) evaluates three standardized points, which are identified by placing both hands side by side on the chest: upper BLUE-point (middle of the upper hand), lower BLUE-point (middle of the lower palm), and PLAPS (posterolateral alveolar and/or pleural syndrome)-point (defined by the intersection of a horizontal line at the level of the lower BLUE-point; a vertical line at the posterior axillary line) (Tables 33.1 and 33.2).

The profile combining A-profile, free veins, and PLAPS is called A-V-PLAPS-profile.

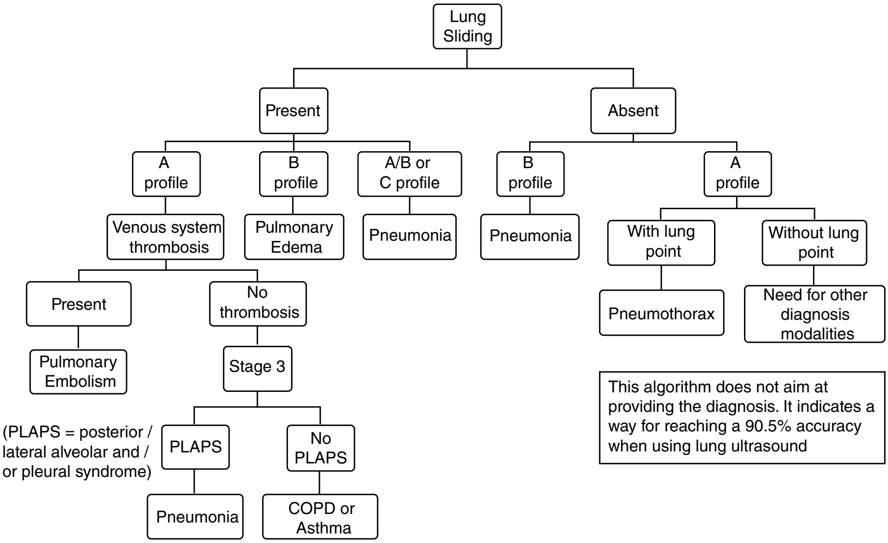

Lung Sliding
Present
Absent
A profile
B profile
A/B or C profile
B profile
A profile
Venous system thrombosis
Pulmonary Edema
Pneumonia
Pneumonia
With lung point
Without lung point
Present
No thrombosis
Pneumothorax
Need for other diagnosis modalities
Pulmonary Embolism
Stage 3
This algorithm does not aim at providing the diagnosis. It indicates a way for reaching a 90.5% accuracy when using lung ultrasound
(PLAPS = posterior / lateral alveolar and / or pleural syndrome)
PLAPS
No PLAPS
Pneumonia
COPD or Asthma

Fig. 33.8 Blue protocol

Table 33.1 Various profiles and their correlation with the pathology

Profile	Definition	Pathological process
A profile	Anterior lung-sliding with A-lines	Normal or if lung sliding absent—pneumothorax If DVT positive—pulmonary embolism If DVT negative with PLAPS—pneumonia If DVT and PLAPS negative—nude profile s/o severe asthma or COPD
B profile	Lung-sliding with lung-rockets	Acute cardiovascular pulmonary edema
B' profile	B-profile with abolished lung-sliding	Pneumonia
C profile	A thickened, irregular pleural line	Pneumonia
A/B profile	Half A-profile at one lung, a half B-profile at another	Pneumonia
PLAPS-profile	Posterolateral alveolar and/or pleural syndrome	Pleural effusion, consolidation, pneumonia

Table 33.2 Various signs and their correlation

Seashore sign	Normal lung
Quad sign or sinusoidal sign	Pleural effusion
Shred sign or tissue-like sign	Consolidation
Lung rockets	Interstitial syndrome
Stratosphere sign or barcode sign	Pneumothorax
Lung point	Pneumothorax

Step 2: Hemodynamic Assessment of Circulatory Failure Using Lung Ultrasound: FALLS-Protocol (Fig. 33.9)

- The FALLS protocol follows Weil and Shubin's classification of shock where it first considers obstructive shock followed by cardiogenic, hypovolemic, and then distributive shock.

Other causes of shock like Abdominal aortic aneurysm (AAA) rupture in someone who comes with an unexplained shock with abdominal pain and a pulsatile mass on palpation can be excluded by scanning the abdomen at the level of the umbilicus in a transverse and longitudinal plain. US has been shown to have excellent accuracy (sensitivity of 95–100% and specificity of 100%) when used as a screening modality for detection of AAA.

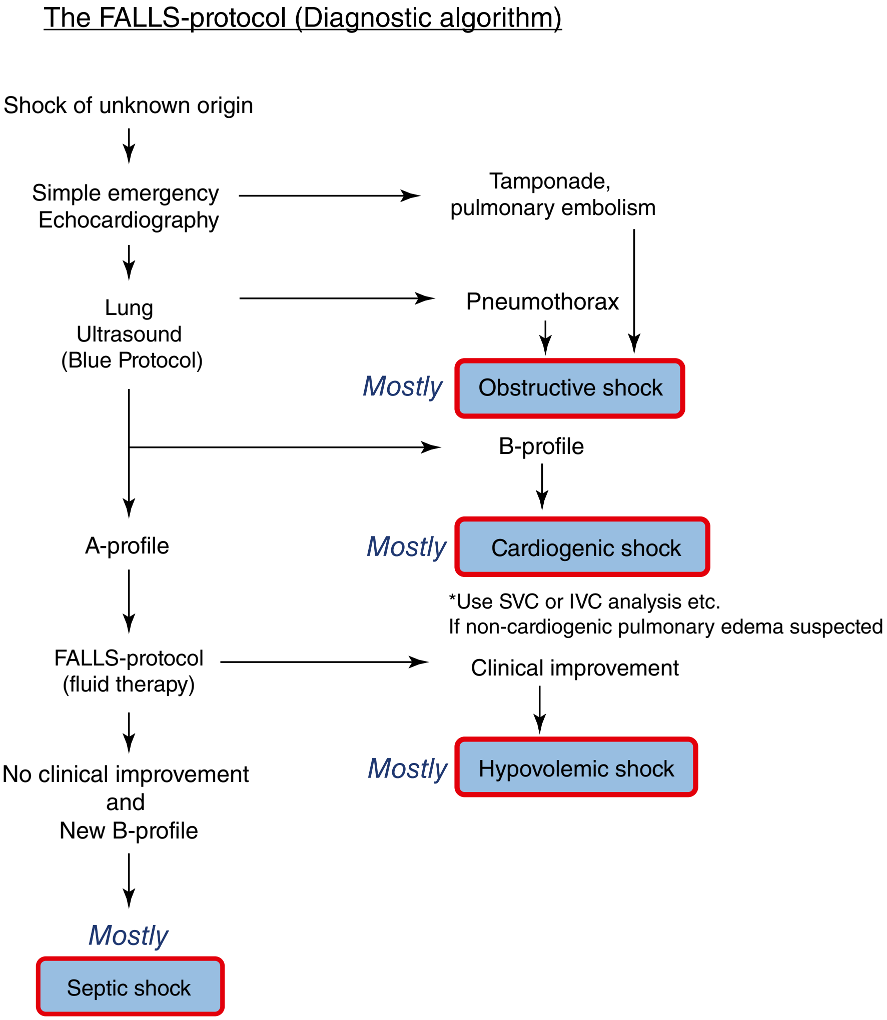

The FALLS-protocol (Diagnostic algorithm)
Shock of unknown origin
Simple emergency Echocardiography
Tamponade, pulmonary embolism
Lung Ultrasound (Blue Protocol)
Pneumothorax
Mostly
Obstructive shock
B-profile
A-profile
Mostly
Cardiogenic shock
*Use SVC or IVC analysis etc.
If non-cardiogenic pulmonary edema suspected
FALLS-protocol (fluid therapy)
Clinical improvement
Mostly
Hypovolemic shock
No clinical improvement and New B-profile
Mostly
Septic shock

Fig. 33.9 The FALLS Protocol

Step 3: Cardiac Ultrasound

The intensivist performs goal-directed echocardiography to know hemodynamic instability in a patient and it differs from the detailed examination of the heart as done by the cardiologist.

Essential Views Using Ultrasound (Table 33.3)

Table 33.3 Essential views using ultrasound

Window	Footprint position	Structures assessed
Parasternal long-axis (PLAX) view	3rd/4th ICS near the sternum with beam toward the right shoulder	Aortic and mitral valvular abnormalities
Parasternal short-axis view	Rotating the transducer to 90 degrees clockwise from the PLAX view and tilting it	EF by eyeballing method mitral valve, papillary muscles, and apex
Apical four-chamber view	At the apex of the heart	Four chambers of the heart along with size and the mitral and tricuspid valves, right ventricular free wall, left lateral wall, interventricular septum
Apical five-chamber view	Tilting of the transducer from the four-chamber view	LVOT and the aortic valve
Subcostal view	Below the xiphoid process	Four chambers along with valvular functions, septal defects, pericardial effusion
Suprasternal view	Suprasternal notch	Aortic flows, arch of aorta with branches, ascending and descending aorta, and pulmonary artery

To Evaluate Hemodynamic Instability in a Patient

Hypotension in ICU patients can be due to hypovolemia, valvular disorders, ventricular dysfunction, or pericardial tamponade. Using point-of-care Echo, several indices can be used to predict fluid responsiveness like inferior vena cava imaging and variation, ventricular size, aortic flow variations, and passive leg raising test.

A. *Inferior vena cava size and variability*
   - Respiratory variations in IVC size can predict fluid responsiveness, both in mechanically ventilated and in spontaneously breathing patients.
   - During spontaneous ventilation, the IVC collapses in inspiration, whereas during mechanical ventilation the IVC dilates during inspiration.
   - IVC distensibility index is measured for fluid responsiveness in mechanically ventilated patients and the IVC collapsibility index in spontaneously breathing patients.
   - A distensibility index of more than 18% in mechanically ventilated and collapsibility of >50% in spontaneous ventilation is indicative of fluid responsiveness. IVC diameter and its respiratory variations are assessed in the subxiphoid ECHO view. It can be measured either close to its entrance to the right atrium (less susceptible to motion artifact but can be influenced by diaphragmatic contraction) or 1–2 cm caudal to the hepatic vein–IVC junction (approximately 3–4 cm from the junction of the IVC and the right atrium; Fig. 33.10).
   - IVC can “inappropriately” collapse in a fluid-resistant patient when the patient is inspiring excessively or the intra-abdominal pressure is abnormally high as in ascites and intra-abdominal hypertension.

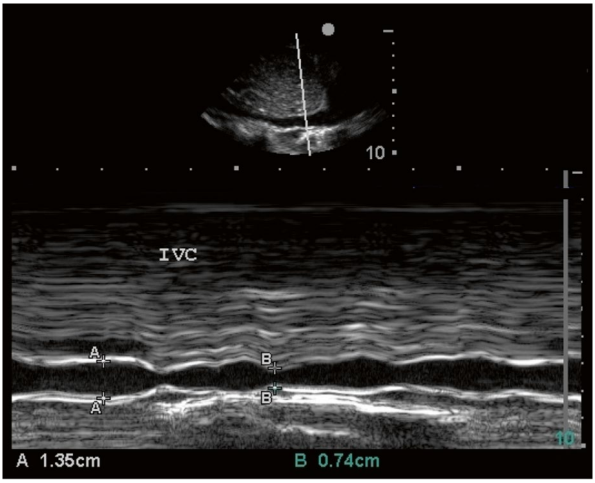


Fig. 33.10 IVC variation with respiration in 2D mode and M mode

B. *Right ventricular dysfunction*

RV dysfunction accompanies a dilated IVC in almost all cases. Right ventricular dilation can be assessed by ultrasound if its size is similar to or larger than the left ventricle. PSAX view will demonstrate flattened interventricular septum, better known as *D-sign* in the case of RV overload states.

C. *Left ventricular dysfunction*

Assess the LV size to determine whether it is dilated or hypertrophied, along with evaluating the ejection fraction and detecting regional wall motion abnormalities. The parasternal short-axis view is particularly effective for detecting RWMA, although this assessment is best performed by a trained intensivist.

D. *Pericardial tamponade* (Fig. 33.11)

Right atrial collapse during ventricular systole and RV diastolic collapse along with the presence of pericardial fluid in hemodynamically unstable patients indicates cardiac tamponade, which is best visualized in the apical four-chamber view or subcostal view.

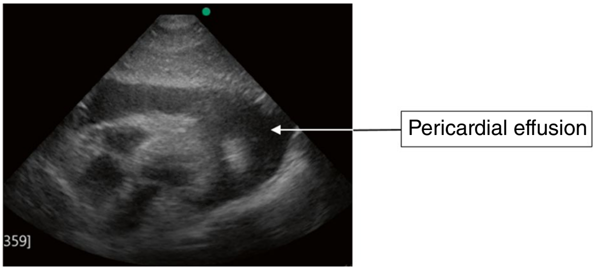


Fig. 33.11 Pericardial tamponade

Step 4: Procedures

- Venous cannulation: IJV or subclavian vein cannulation can be done by out-of-plane or in-plane technique. In-plane technique is one where the entire length of the needle penetrates the soft tissue until the vein is seen during cannulation, which minimizes the risk for arterial puncture and pneumothorax. Out-of-plane technique is where the needle is directed toward the plane of the ultrasound beam and only the tip of the needle is followed until the vessel is cannulated.
- Ultrasound guidance arterial cannulation minimizes the number of attempts as well as shortens the procedure time.
- Thoracentesis and abdominocentesis.
- Percutaneous tracheostomy to exclude the presence of vascular structures and visualizing the course of needle and guidewire insertion.

Step 5: Evaluation of DVT

- Use the three-point compression test to assess for DVT by evaluating the common femoral vein, proximal deep femoral vein, and popliteal vein. Lack of compressibility of the veins during scanning suggests the presence of DVT.

Step 6: FAST Protocol—Focused Assessment of Sonography in Trauma

- Assesses four areas for fluid collection: hepatorenal pouch (Morrison's pouch), splenorenal recess, pelvic space, and pericardial space. When the lungs are assessed for pneumothorax or hemothorax alongside the FAST scan, it is referred to as eFAST (Table 33.4).

Table 33.4 FAST protocol

Quadrant	Transducer position	Structures identified
RUQ	Right subcostal, anterior axillary line Mid axillary line approx. in 7th ICS	Liver Diaphragm Kidney Hepatorenal recess
LUQ	Left subcostal, anterior axillary line Mid-posterior axillary line in 7th ICS	Spleen Kidney Lung Diaphragm Splenorenal recess
Subcostal	Below the xiphoid process	IVC, pericardial collection
Pelvic	Above pubis with inferior angulation	Bladder, uterus, prostate, cul de sac, rectovesical space

Step 7: Ultrasound in Cardiac Arrest

- This is for patients receiving CPR to rule out potential reversible causes of cardiac arrest like pneumothorax, cardiac tamponade, and pulmonary embolism along with assessing the contractility of the heart.

Step 8: Examine Surrogates for Increased ICP

Optic nerve sheath diameter (ONSD) is normally less than 5.0 mm in diameter. Using the linear transducer over the eyelid, measure the optic nerve sheath diameter at a distance 3 mm posterior to the globe. It has a good negative predictive value, i.e., if less than 5.7 mm, then the ICP is unlikely to be more than 20 mmHg.

B-mode transcranial color-coded duplex (TCCD) insonation of MCA (middle cerebral artery) can be used to measure the pulsatility index and diastolic flow velocities, to rule out intracranial hypertension, detect signs of brain death, and evaluate for vasospasm.

Step 9: Renal Ultrasound

POCUS allows for the detection of hydronephrosis, volume of urine in the urinary bladder, and urinary distention, aiding in the decision for catheterization. Using a convex probe along the lower intercostal space in the mid-axillary line, with a transducer directed posteriorly, helps rule out hydronephrosis, which appears as an anechoic area within the normally echogenic renal sinus.

Conclusion

US has the potential to become a reference tool for bedside head-to-toe diagnosis, dynamic monitoring, and guide therapy in the ICU. It is noninvasive, easily repeatable, and provides rapid and accurate evaluation of the patient's physiological state. It minimizes radiation exposure to medical personnel. Standardized training and systematic use should be advocated to fully utilize its potential.

Suggested Reading

Lichtenstein D. Lung ultrasound in the critically ill. Curr Opin Crit Care. 2014;20(3):315–22.

Lichtenstein DA. BLUE-protocol and FALLS-protocol: two applications of lung ultrasound in the critically ill. Chest. 2015;147(6):1659–70.

Messina A, Robba C, Bertuetti R, et al. Head to toe ultrasound: a narrative review of experts' recommendations of methodological approaches. J Anesth Analg Crit Care. 2022;2:44. https://doi.org/10.1186/s44158-022-00072-5.

Staub LJ, Mazzali Biscaro RR. Lung ultrasound for the emergency diagnosis of pneumonia, acute heart failure, and exacerbations of chronic obstructive pulmonary disease/asthma in adults: a systematic review and meta-analysis. J Emerg Med. 2019;56(1):53–69.

Zieleskiewicz L, Muller L, Lakhal K. Point-of-care ultrasound in intensive care units: assessment of 1073 procedures in a multicentric, prospective, observational study. Intensive Care Med. 2015;41(9):1638–47.

Extracorporeal Life Support

34

Vivek Gupta, Arpan Chakraborty,
and Nilanchal Chakraborty

Case Vignette

A 35-year-old male with a connective tissue disorder presented with a 3-day history of shortness of breath. On evaluation patient was found to be hypoxic (oxygen saturation of 46%), with severe respiratory distress. The patient was intubated and initiated on lung protective ventilation. HRCT thorax followed by bronchoscopy proved diffuse alveolar hemorrhage. In view of persistent hypoxemia and a P/F ratio of 55 mmHg, the patient was initiated on prone ventilation. After 6 h of prone ventilation, the patient was on FiO_2 of 1.0, respiratory rate of 32/min, and tidal volume of 6 ml/kg, and arterial blood gas (ABG) revealed pH 7.19, pCO_2 75 mmHg, pO_2 56 mmHg, and SaO_2 78%.

Extracorporeal membrane oxygenation (ECMO) is the only treatment modality currently available that can completely replace the cardiorespiratory function and remains the rescue therapy of choice for refractory hypoxemia in patients with severe acute respiratory distress syndrome (ARDS). The use of ECMO for worsening oxygenation has been on the rise since the H1N1 influenza pandemic in 2009. Veno-venous ECMO (VV ECMO) is preferred unless the patient is in septic shock or has associated myocardial dysfunction leading to cardiogenic shock. In these circumstances, veno-arterial ECMO (VA ECMO) can be considered.

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Step 1: Planning for ECMO

- Initiate discussion with family members of the patient for probable need of ECMO immediately when other rescue ventilation methods are failing and the ECMO team should be communicated regarding potential ECMO patient.
- Percutaneous ECMO cannulation trolley should be checked for the following items:
  - Measuring tape to estimate height, predict weight, and cardiac output
  - ECHO/USG machine
  - Appropriate size drainage and return cannulas
  - J tipped Guide wires (0.035–0.038 in, 150–180 cm long)
  - Dilators of various sizes (8F–26F)
  - 11-size surgical blades
  - Sterile surgical whole-body drapes
  - Isotonic crystalloid solution
  - Heparin
  - Sutures (non-absorbable)
  - Large transparent dressings
  - 3-way stopcocks
  - Pressure monitoring kits
- Continue with lung protective ventilation throughout before initiating ECMO, with a target plateau pressure of less than 30 and driving pressure of less than 15.

Step 2: Indication of ECMO

- Patients with severe but potentially reversible acute respiratory or cardiac failure that is unresponsive to conventional management are suitable candidates for ECMO.
- For patients who are in a medical center not equipped with ECMO, transfer to ECMO-equipped medical center should be considered, ideally after the referral team has assessed the patients and if necessary transfer on ECMO.
- *Inclusion criteria for Extracorporeal Cardiopulmonary Resuscitation:*
  1. Age less than 70 years
  2. Cardiopulmonary arrest to initiation of CPR (no flow time) less than 5 min
  3. Witnessed arrest
  4. Ventricular fibrillation or paroxysmal ventricular tachycardia or pulseless electrical activity (PEA) as initial cardiac rhythm
  5. Recurrent VF intermittent ROSC
  6. Absence of any comorbidity like COPD, liver failure, end-stage heart failure, or terminal irreversible disease
  7. No known aortic valve incompetence

- *Indication for VV ECMO:*
  1. Hypoxic respiratory failure
     (a) After optimal medical management, after a trial (maximum of 6 h of prone ventilation), if the patient's blood gas reveals the following parameters:
     (b) P/F <80 mmHg with $FiO_2 > 0.8$
     (c) ECMO can also be initiated after 3 h of prone ventilation if the P/F ratio remains less than 50 mmHg with $FiO_2 > 0.8$
  2. Hypercapnic respiratory failure despite mechanical ventilation despite high P_{plat} (>30 cm H_2O)
     (a) pH <7.25 with pCO_2 >60 mmHg after conventional mechanical ventilation (respiratory rate 35 beats per minute and plateau pressure [P plat] ≤30 cm H_2O)
  3. As a bridge to lung transplant or primary graft dysfunction following a lung transplant
     (a) Specific clinical condition:
        (i) Viral/bacteria/pneumonia and aspiration causing acute respiratory distress syndrome
        (ii) Acute eosinophilic pneumonia
        (iii) Diffuse alveolar hemorrhage
        (iv) Status asthmaticus
        (v) Severe inhalational injury
        (vi) Large bronchopleural fistula
        (vii) Severe air leak syndromes
        (viii) Extracorporeal assistance to support the lung in cases of airway obstruction, pulmonary contusion, drowning, and smoke inhalation
        (ix) Immediate cardiac or respiratory collapse (PE, blocked airway, unresponsive to optimal care)
  - *Indication for VA ECMO:*
    1. Cardiogenic shock characterized by systemic systolic pressure less than 90 mmHg, urine output less than 30 ml/h, lactate over 2, SVO2 less than 60%, or altered conscious state for 6 h unresponsive to optimal treatment.
- *Contraindications for ECMO*
  – The sole absolute contraindication for starting ECMO is expected non-recovery without a feasible decannulation plan.

Relative contraindications include

  – Older age
  – Mechanical ventilation more than 7 days with P_{plat} more than 30 cm H_2O and FiO_2 more than 90%
  – Contraindication for anticoagulation (high bleeding risks, expanding intracranial hemorrhage)
  – Comorbid conditions like terminal malignancy, severe brain injury, and immunosuppressed patients

Step 3: Selection of Cannula

- Assess the vessels (femoral and jugular) for diameter and flows: the size of the drainage cannula should not be more than 2/3rd of the total diameter of the femoral vein.
- Measure patient's cardiac output by echocardiography: cannula size should accommodate the highest ECMO flows possible (at least 60% of native cardiac output) with the least revolutions per minute on the ECMO machine.
- Essentially, ECMO cannulas should be short and fat.
- Appropriate size cannula will allow sufficient ECMO flow at maximum speed for the given pump.
- In an adult person:
  - Drainage cannula: 23–25 Fr
  - Reinfusion cannula: 17–21 Fr
- Multistage drainage cannula is preferred. Each cannula has M numbers, which suggest the maximum flow that can be achieved with the particular size of cannula.
- Kink-free reinforced cannulas with heparin/bioline coating should be used.

Step 4: Percutaneous ECMO Cannulation

- Things to be considered before cannulation:
  - Cannula access feasibility
  - Cannula size
  - Efficiency of the chosen VV mode
  - Performance of the right ventricle
  - Biventricular function
  - Predicted duration of support
- Can be done by critical care physicians, cardiologists, emergency physicians, and cardiac surgeons.
- The cardiac surgical team should always be available at the cannulation site, for rescue surgical cannulation if the percutaneous approach fails.
- Configuration of VV ECMO: separate draining and perfusion cannula, either femoro-femoral, jugulo-femoral, or femoro-jugular, are still the most frequently used.
- Percutaneous cannulation should always be done under ECHO/USG or fluoroscopy guidance. When USG guidance is not available, anatomical landmark techniques must be used, venous placement can be confirmed using the transducer.
- Femoro-Jugular VV ECMO:
  - Tip of drainage cannula: junction of inferior vena cava and right atrium
  - Distance between drainage and reinfusion cannula: at least 10–15 cm to minimize reperfusion
- Double lumen cannula:
  - Tip of cannula: in the inferior vena cava
  - Reinfusion: in the right atrium pointing anteromedially toward the tricuspid valve

Step 5: Initiation of VV ECMO

Pre-ECMO Check List

- The cannula should be well secured and without bleeding.
- All connectors should be adequately tightened and preferably have a tie gun.
- All ports should be blocked.
- Pressure tubing and pressure line connected.
- Patient's vitals should be noted including ABG, lactate, and CBC.
- A bolus dose of heparin must be given.
- Blood products (PRBC) must be available.
- The circuit should be primed properly and is de-aired and running with the flow of 300 ml/min.
- ACT machine should be available.
- Crash cards and emergency medicines should be available.
- Venous end of the circuit should be connected to the venous cannula and the arterial end should be connected to the venous cannula.

Protocol for Initiation

- The pump should be started at RPM 1200 to target flow 20 ml/kg/min and gradually increase the flow every 5–10 min by 10 ml/kg/min up to the desired flow.
- The gas flow to blood flow ratio should be 0.5:1 and FiO_2 must be 100% on ECMO.
- The color of the venous and arterial cannula should be checked for color difference.
- The heater–cooler unit should be attached to the oxygenator.
- Prepump, preoxygenator, and postoxygenator pressures should be checked.

ECMO Settings

- ECMO flow and inspired oxygen on the membrane: titrated to target PaO_2 of at least 60 mmHg.
- ECMO flow—increase slowly to avoid hypotension on initiation.
- Target ECMO flow—at least 60% of native cardiac output. ECMO flows should be increased until the target oxygenation is achieved.
- Sweep gas flow: at initiation, sweep gas flows should be as low as possible. During ECMO initiation, a sweep gas flow of 2 l is recommended.
- Sweep gas can be titrated gradually based on pH and pCO_2. Rapid correction of CO_2 should be avoided as it increases the risk of intracranial hemorrhage.
- Once the desired flow has been achieved, ventilator settings should be lowered down.

- Prepump pressure normally should be less than −20 mmHg, and post-oxygenator pressure must be kept less than 300 mmHg.
- *Mechanical ventilation settings*
- Ultra-lung protective ventilation.
- Respiratory rate: 5–10 breaths/min.
- Tidal volume: 1–3 ml/kg.
- Plateau pressure: <20 cm H_2O.
- PEEP: at least 10 cm H_2O is suggested to decrease LV afterload and prevent or treat pulmonary edema.
- FiO_2: less than 50%.

Step 6: Anticoagulation and Blood Product Management on VV ECMO

- The first choice is heparin as it has a rapid onset of action and is easily reversible in pediatric and adult patients.
- Heparin/bioline-coated circuits should be used to minimize the need for anticoagulation.
- The initial bolus dose of heparin should be 75–100 units/h.
- The maintenance dose should be started with 20 units/kg/min.
- Bivalirudin and argatroban can be used in patients with heparin-induced thrombocytopenia or when the patient is allergic to heparin.
- Starting dose of argatroban: 0.2–0.5 mcg/kg/min and the dose of bivalirudin: 0.025–0.05 mg/kg/min.

Anticoagulation monitoring parameters (with heparin anticoagulation)

- ACT (Activated Clotting Time)
  - Most commonly used, before initiation on heparin, 1 h after initiation, every 4 hourly when on a heparin drip.
  - It is a measure of whole blood clotting.
  - Deranged ACT could be because of various factors other than anticoagulation:
    - Excessive anticoagulation
    - Thrombocytopenia
    - Coagulopathy
    - Liver or renal dysfunction
    - Hypothermia
- aPTT (Activated Partial Thromboplastin Time)
  - Measures both intrinsic and final common pathways of coagulation.
  - Deranged aPTT is seen in the following factors, other than heparin anticoagulation:
    - Lupus anticoagulant
    - Deficiency of coagulation factors

- Anti-Xa activity
  - Assay of anti-Xa is dependent on heparin anticoagulation and anti-thrombin levels.
  - It is used to measure the plasma level of heparin.
  - Not influenced by any other parameter.
- Thromboelastography can be used for anticoagulation monitoring.
- Anticoagulation targets:
  - ACT: 160–180 s
  - aPTT ratio: 1.5–2 times the normal value
  - Anti-Xa levels: 0.3–0.7 IU/ml
- VV ECMO at high ECMO flows (>4 l/min) can be maintained with minimal to no anticoagulation, especially in patients with a high risk of bleeding.
- ECMO flows of 2.5 l/min or less have an extremely high risk of thrombosis and thus necessitate higher anticoagulation.
- Anti-thrombin III activity should be checked in patients who require high doses of heparin, to achieve a given anticoagulation target. Target range is more than 70%.
  - Causes of decreased level
  - DIC
  - Microangiopathic hemolytic anemia
  - Chronic liver disease

Blood product management (Table 34.1)

- Protocol for blood product transfusion

- If the patient develops massive life-threatening coagulopathy, the entire ECMO unit should be changed.

Table 34.1 Blood component therapy on ECMO

	Management	
Blood component	ELSO (Extracorporeal life support organization recommendation)	Recent evidence
Platelets	In the case of bleeding transfuse <75,000/mm^3 If no bleeding: transfuse if <30,000/mm^3	
Fresh frozen plasma	Transfuse if INR >2 Low antithrombin	No new evidence
Fibrinogen	Transfuse cryo-precipitate to maintain fibrinogen >100 mg/dl Dose is 15 ml In bleeding patients, target >150 mg/dl	If fibrinogen persistently <100 mg/dl, consider changing the ECMO circuit
Red blood cells	Target hematocrit of 30%	No higher targets are needed on ECMO. Transfuse when Hb is <7 g%

Step 7: Clinical Care on ECMO

1. *Sedation and ventilation*
    - Continue with deep sedation with or without neuromuscular blockage for an initial 24–48 h on ECMO.
    - Most of the sedatives get adsorbed by the circuit; hence, their dose requirement is usually high.
    - The patient can be initiated on spontaneous respiration at the earliest, with targets of lung protective to ultra-lung protective ventilation.
    - Aggressive physiotherapy of the chest and limbs is to be performed routinely.
    - The patient should be mobilized at the earliest possible opportunity and all measures to prevent ventilator-associated pneumonia should be carried out.
    - Assess every day for the readiness of weaning from ECMO and the ventilator.
2. *Nutrition*
    - Enteral nutrition should be initiated at the earliest and nutrition care should be the same as any critically ill patient.
    - Target caloric intake: 60–90 per kg per day.
    - Glycemic control should be achieved with target blood sugars of 140–180 mg/dl.
3. *Antibiotics*
    - Incidences of secondary sepsis are almost 20% with the patient on ECMO.
    - Fever may not be there as the patient is on ECMO.
4. *Drug dosing*
    - Significant alterations in drug pharmacokinetics occur in patients on ECMO.
    - Most common ones include:
        - Increased volume of distribution
        - Absorption of the drug to the ECMO circuit and membrane, leading to enhanced clearance
        - Renal dysfunction and non-pulsatile flow, leading to reduced clearance
    - Appropriate dosing of drugs is of paramount importance and drug monitoring should be used whenever indicated clinically.
5. *Fluid management*
    - Most of the patients are fluid loaded but sometimes may be intravascularly depleted due to capillary leak syndrome, high flow ECMO, bleeding, or diuresis.
    - It is difficult to assess fluid status by CVP or pulmonary artery pressure due to ECMO flow. Fluid status can be determined by
        - Too negative pre-membrane pressure
        - Response to fluid challenge
        - Maintenance fluid requirement is 80–100 ml/kg/day.

Step 8: Monitoring and Trouble Shooting on ECMO

1. *Clinical monitoring*
    - Every ECMO patient should be examined from head to toe, drainage cannula to reinfusion cannula at least once during every shift and as and when required.
    - Clinically look for the following:
        - – Insertion sites of cannula for infection, and bleeding
        - – Circuit for signs of thrombosis
        - – Color difference of the blood in the inflow and outflow tubings of the ECMO circuit. If the color difference is minimal, one should rule out recirculation and also check if the sweep gas is disconnected or turned off
        - – An emergency blood product supply should be maintained
        - – Chattering of the ECMO tubings
        - – Membrane: for thrombosis and fibrin deposition
        - – Pressure sores
        - – Perfusion of limbs: signs of ischemia, discoloration, and mobility
2. *Monitoring on ECMO console*
    - Mode on the ECMO machine
    - Power connection on the ECMO console
    - Charge on the battery (battery backup)
    - ECMO flows
    - RPM (revolution per minute)
    - Temperature on the heat exchanger
    - Sweep gas flows, gas connection
    - Inspired oxygenation to the membrane
    - Tubing clamps preferably guarded must be available on the pump cart; minimum 6–8 clamps
3. *Blood gas analysis and ventilation*
    - Arterial blood gases: one hour after and then as clinically indicated.
    - Ventilatory parameters: tidal volume, plateau pressure, driving pressure and peep should be routinely monitored.
    - Trans pulmonary pressure guided ventilator management can be considered, if available.
    - Spontaneous ventilation is always preferable.
    - Sweep gas should be adjusted to achieve PCO_2 up to 30 with respiratory rate 30–34/min if respiratory rate is high on spontaneous ventilation.
    - Central venous oxygen saturation ($ScvO_2$):
        - – Certain ECMO machines have in-built monitoring of central venous saturation.
        - – Routine monitoring of $ScvO_2$is not required.
        - – High $ScvO_2$ is a marker of recirculation.
4. *Anticoagulation lab*
    - The anticoagulation lab schedule is discussed in Table 34.2.
    - Plasma-free hemoglobin (PFH):
        - – Should be measured every day in patients with ECMO.

Table 34.2 Anticoagulation monitoring

Parameter	Frequency of monitoring
ACT	After one hour of initiation of ECMO Once stabilized—every 4 h
APTT ratio	Every 4–12 h initially Once stabilized, daily
Anti-Xa levels	Once stabilized, daily
Platelets	Every 12 h and as needed
Fibrinogen	Once daily
Plasma-free hemoglobin	Once daily
Anti-thrombin III assay	As and when needed
Thromboelsatography	As and when needed
Hemoglobin	Before and after starting ECMO Twice a day

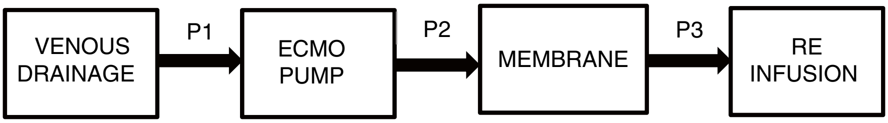

Fig. 34.1 ECMO circuit pressure monitoring

  - Higher PFH (>5 g/dl) is an indicator of significant hemolysis and needs immediate steps to identify the cause and initiate corrective measures.
  - Cause of high PFH (high hemolysis):
    - Hypovolemia
    - Position of drainage cannula—too low in the inferior vena cava
    - Small drainage cannula
    - Thrombosis of the membrane
    - Repetitive episodes of chattering of the lines

5. *Other laboratory tests*
   - Blood cultures should be sent as per the clinical need.
   - Renal function tests and electrolytes—as and when appropriate.
   - Liver function tests—as and when clinically appropriate.
   - All other tests as deemed necessary according to the clinical profile of the patient.
6. *ECMO circuit pressure monitoring*
   - The interfaces where pressure monitoring should be done on ECMO are explained in Fig. 34.1.

- P1: inflow pressure into the pump and is always negative:
  - Normal range up to −20 mmHg.
  - Alarm limit should be set at −70 mmHg.
  - Causes of increased negative pressure are poor catheter placement, low volume, and inadequate cannula size, which should be addressed.
- P2: pressure between the pump and membrane oxygenator. It is the pressure generated by the non-occlusive pump to propel blood forward:

Table 34.3 Circuit pressure monitoring

P1	P2	P3	Cause
↓	↓	↓	Hypovolemia, tension pneumothorax, tamponade, kinking, or malposition of drainage cannula
↑/N	↓	↓	Pump failure
↑/N	↑/N	↓	Oxygenator failure (thrombosis)
↑/N	↑	↑	Increased afterload, hypertension, kinking, or malposition of infusion cannula

  - Depends on the size of the oxygenator and its surface area.
  - P2 is always positive, with normal values ranging from 150 to 280 mmHg depending on ECMO flows.
  - Depends on the blood flow rate—the more the flow, the more the pressure.
  - Clogging of the oxygenator will increase the pressure.
- P3: pressure post-membrane:
  - The difference between P2 and P3 (membrane pressure drop) should always be less than 50 mmHg.
  - Depends on the blood flow rate—the more the flow, the more the pressure.
  - Clogging of the oxygenator will decrease the pressure.
  - Higher pressure drops suggest membrane thrombosis.
  - Post-membrane pressure should be kept below 300 mmHg in order to minimize the risk of hemolysis and plasma breakthrough.
- The various reasons for the changes in pressures are discussed in Table 34.3.

7. *Radiological investigations*
   - Chest X-ray:
     - To check for the position of ECMO cannulas
     - Radiological improvement in lung parenchyma
     - Position of other tubings like endotracheal tube, central venous lines, nasogastric tubes, etc.
     - Identification of pleural effusions, pneumothorax
   - Ultrasonography and echocardiography:
     - Check for lung parenchyma, pneumothorax, and pleural and pericardial effusion
     - Position of ECMO cannulas
     - Evidence of venous thrombosis and pseudoaneurysm
     - Cardiac output of the patient
     - Volume status of the patient
     - Examination of valves—especially tricuspid for fungal endocarditis

Step 9: Hypoxemia on VV ECMO

- There is no defined cutoff for hypoxemia on ECMO.
- Patients with SaO_2 of less than 80 despite best ECMO optimization should be considered to be hypoxic.

- A fraction of patients would continue to remain hypoxic despite initiation of ECMO and a fraction of them will develop episodes of significant hypoxemia during the treatment period.
- A simplified algorithm (Figs. 34.2 and 34.3) explains the approach to identify the cause of hypoxemia on VV ECMO and hypotension (Fig. 34.4).

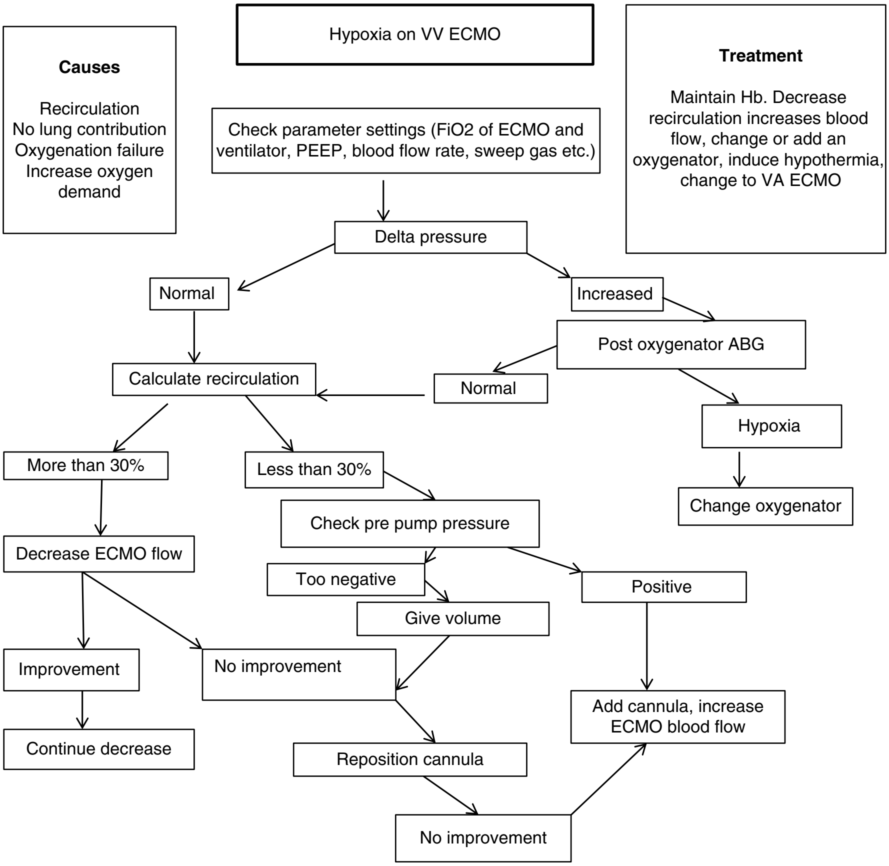
Causes
Recirculation
No lung contribution
Oxygenation failure
Increase oxygen demand
Hypoxia on VV ECMO
Treatment
Maintain Hb. Decrease recirculation increases blood flow, change or add an oxygenator, induce hypothermia, change to VA ECMO
Check parameter settings (FiO2 of ECMO and ventilator, PEEP, blood flow rate, sweep gas etc.)
Delta pressure
Normal
Increased
Post oxygenator ABG
Calculate recirculation
Normal
Hypoxia
Change oxygenator
More than 30%
Less than 30%
Check pre pump pressure
Decrease ECMO flow
Too negative
Positive
Give volume
Improvement
No improvement
Add cannula, increase ECMO blood flow
Continue decrease
Reposition cannula
No improvement

Fig. 34.2 Hypoxia algorithm on VV ECMO

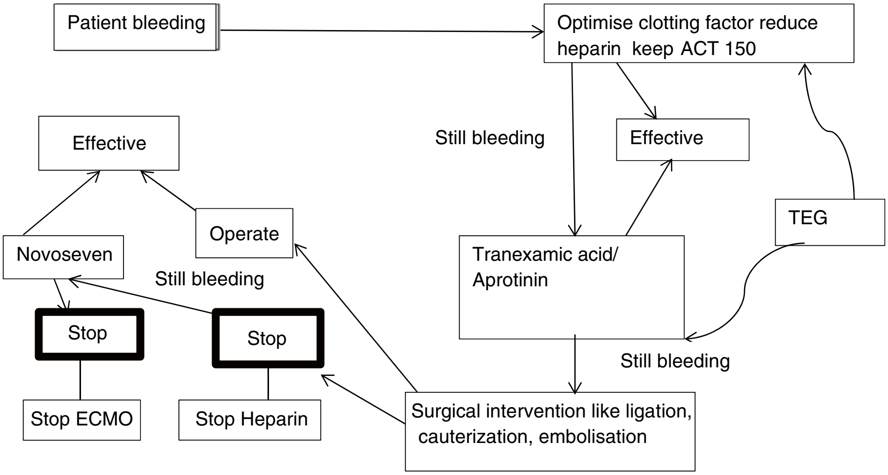
Patient bleeding
Optimise clotting factor reduce heparin keep ACT 150
Still bleeding
Effective
TEG
Effective
Operate
Novoseven
Still bleeding
Tranexamic acid/ Aprotinin
Stop
Stop
Still bleeding
Stop ECMO
Stop Heparin
Surgical intervention like ligation, cauterization, embolisation

Fig. 34.3 Protocol for bleeding patient on ECMO

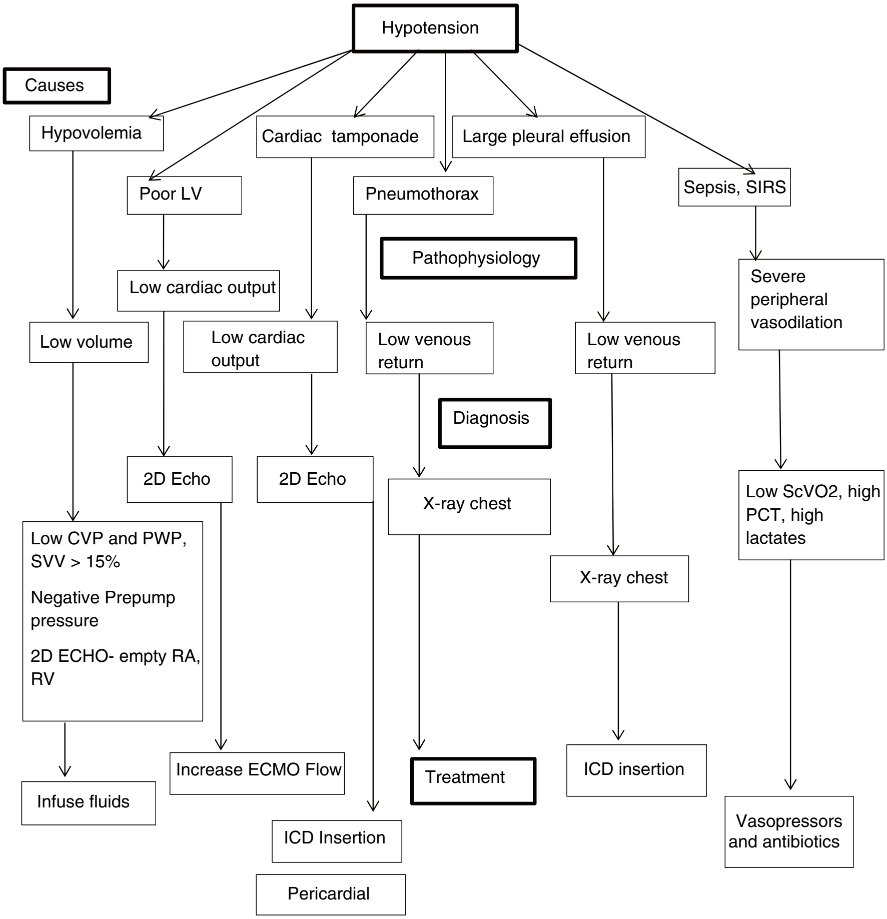
Hypotension
Causes
Hypovolemia
Cardiac tamponade
Large pleural effusion
Poor LV
Pneumothorax
Sepsis, SIRS
Pathophysiology
Low cardiac output
Severe peripheral vasodilation
Low volume
Low cardiac output
Low venous return
Low venous return
Diagnosis
2D Echo
2D Echo
X-ray chest
Low ScVO2, high PCT, high lactates
Low CVP and PWP, SVV > 15%
Negative Prepump pressure
2D ECHO- empty RA, RV
X-ray chest
Increase ECMO Flow
Treatment
ICD insertion
Infuse fluids
Vasopressors and antibiotics
ICD Insertion
Pericardial

Fig. 34.4 Approach to a patient with hypotension on ECMO

Step 10: Weaning from VV ECMO

- The weaning trial can be considered once the support on ECMO is less than 30% of total lung function, usually 3 l/min in adults.
- Criteria for trial off:
  - Acceptable blood gases and tissue perfusion on 21% FdO_2 and minimal sweep gas
  - ABG on moderate ventilator settings showing
    - PO_2 more than 70 mmHg
    - PCO_2 less than 50 mmHg
    - Normal pH
  - Stable hemodynamics
  - Improving lung compliance, generating a tidal volume of more than 5 ml/kg with a peak pressure of less than 26
- Stepwise weaning protocol
  - Step I
    - Reduce FdO_2 of ECMO by 5% every 3–4 h until 50%
    - Maintain SpO_2 more than 92%
    - Once FdO_2 has reached 50%, increase ventilator settings to a moderate level: FiO_2 40% and PEEP 8–10 cm H_2O
  - Step II
    - Reduce FdO_2 of ECMO by 5% every 2 h until FdO_2 21%
    - Maintain SpO_2 92%
  - Step III
    - Decrease sweep gas by 0.8 L/min every 2 h until it reaches 0.5 l/min
    - Heparin/ACT should be maintained at the same level
- Monitor HR, BP, PaO_2, and $PaCO_2$, and look for evidence of reduced tissue oxygenation like lactates and $ScvO_2$.
- PaO_2 >60 mmHg, with acceptable carbon dioxide levels and normal tissue oxygenation, is an indicator that the patient can be weaned off from VV ECMO.
- The patient should be stable for a minimum of 4 h before considering decannulation.
- Trial off can be given for 12–24 h if the patient tolerates it.

Step 11: ECMO Decannulation

- The surgical team should be ready.
- Stop heparin anticoagulation for at least half an hour.
- Measure ACT or aPTT before decannulation.
- ACT should ideally be less than 150 s.
- Percutaneous cannulas can be just pulled out, followed by the application of horizontal matrix sutures and compression for over 30 min.
- Ask the patient to perform a Valsalva maneuver to minimize the risk of air embolism during decannulation.
- Observe the patient for at least 6 h before mobilizing the limb and patient.

Step 12: Critical Care Post-ECMO

- Every aspect of critical care should continue.
- Aggressive chest rehabilitation should be pursued.
- Daily examination of vessels for evidence of thrombosis and pseudo aneurysm should be done.

Suggested Reading

Brogan TV, Lequier L, et al. Extra corporeal life support: the ELSO red book. 5th edition. *This book is the official text of extracorporeal life support organization.*

Combes A, Hajage D, et al. Extracorporeal membrane oxygenation for severe acute respiratory distress syndrome. N Engl J Med. 2018;378:1965–75. *In patients with severe ARDS, there was no significant difference in 60-day mortality with ECMO than with a strategy of conventional mechanical ventilation that included ECMO as a rescue therapy.*

Mossadegh C, Combes A. Nursing care on ECMO. *Comprehensive text on nursing aspects of ECMO patients.*

Peek GJ, et al. Efficacy and economic assessment of conventional ventilatory support versus extracorporeal membrane oxygenation for severe adult respiratory failure (CESAR): a multicentre randomised controlled trial. Lancet. 2009;374:1351–63. *This study concluded that in severe but potentially reversible respiratory failure, whose Murray score exceeds 3.0 or who have a pH of less than 7.20 on optimum conventional management, they should be transferred to a center with ECMO-based management to significantly improve survival without severe disability.*

Sangalli F, Patroniti N, Pesenti A. ECMO – extra corporeal life support in adults. *Simplified textbook, describing in brief every aspect of ECMO.*

Environmental Hazards and Disaster Management

35

Jagdish Dureja, Sangeeta, Prateek, and Pranav Bansal

Heat Stroke

Case Vignette

In the middle of June, a 65-year-old male laborer was found unconscious at a work site. On examination, he was found to be obtunded with minimal response to painful stimuli. His skin was hot and flushed. He was tachypneic, tachycardic, hypotensive, and hyperthermic (core temperature 107 °F or 41.7 °C).

Normothermia is a fine equilibrium between heat production and dissipation. Heat-associated illnesses extend from heat exhaustion to heat stroke. Hyperthermia is defined as body temperature >40 °C. Hyperthermia can have grave consequences such as renal failure, disseminated intravascular coagulation, and even death. The outcome significantly depends on prompt and appropriate management.

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https://doi.org/10.1007/978-981-96-5636-3_35

Step 1: Initiate Resuscitation

- These patients should be resuscitated as mentioned in Chap. 24.
- Administer IV fluids promptly as these patients have severe dehydration.
- The type and amount of fluid should be guided by volume status, electrolytes, and cardiac functions.
- The role of point-of-care ultrasonography (POCUS) in identifying the severity of volume deficit in such patients is of paramount importance.
- To avoid peripheral vasoconstriction, vasopressor use should be reserved for patients in whom hemodynamic instability is not improved with volume resuscitation.

Step 2: Assess the Cause and Type of Hyperthermia by History and Examination

- Hyperthermia may be caused by infection, sepsis, tetanus, malaria, toxic ingestions, central nervous system disorders, and heat waves.
- Severe hyperthermia (>40.5 °C or > 105 °F) is usually caused by heat stroke, malignant hyperthermia, and neuroleptic malignant syndrome.
- Exertional heat stroke is usually caused by prolonged exposure to excessive levels of perceived heat. Core temperatures exceeding 104 °F (40 °C) indicate thermoregulatory failure.
- Exertional heat stroke occurs in young, healthy individuals engaged in heavy exercise during periods of high ambient temperature and humidity.
- Non-exertional heat stroke is diagnosed with a core temperature of >40 °C and central nervous system dysfunction. It may be precipitated by exposure to severe environmental heat or medications like anticholinergic drugs, antihistamines, antipsychotics (e.g., MAO inhibitors and TCA), neuroleptic agents, and illicit drugs (amphetamines, cocaine, LSD, MDMA) as these drugs affect vasodilation, sweating, and other heat-loss mechanisms. Other causes include brain hemorrhage, status epilepticus, thyrotoxicosis, and pheochromocytoma.
- Heat exhaustion is a relatively milder form of heat-related disorder that presents with excessive sweating and exhaustion after heat exposure and is not associated with CNS symptoms, electrolyte disorder, and organ dysfunction, but may progress to heat stroke if not properly managed. Advise rest in a cool and well-ventilated place and offer fluids (precluding alcohol and caffeine).
- Encourage him/her to shower and bath, or sponge off with cool water.
- Malignant hyperthermia is a rare complication associated with general anesthetics such as succinylcholine and halothane.
- Signs and symptoms of heat stroke include dry skin, pupillary dilatation, altered mentation, seizures, hallucinations, delirium, tachypnoea, rales due to noncardiogenic pulmonary edema, tachycardia, hypotension, arrhythmias, rhabdomyolysis, dyselectrolytemia, and coma. Disseminated intravascular coagulation and mixed respiratory and metabolic acidosis can also accompany the elevated temperature.

Step 3: Send Investigations

- Complete hemogram.
- Creatine phosphokinase—elevated levels suggest rhabdomyolysis.
- Renal function tests.
- Urine for myoglobin.
- Coagulation studies, toxicological screening, CT head, and lumbar puncture.
- Diagnosis of malignant hyperthermia is confirmed by an in vitro muscle contracture test.

Step 4: General Management

- Adequate airway protection, assisted breathing if needed, and support circulation.
- Isotonic saline is the fluid of choice for resuscitation.
- Vasopressors should be avoided.
- The definitive management is total body cooling.
- Patients suffering from heat stroke should be exposed completely, and intravenous access established for medical management.
- Intravenous fluid should be titrated using vital signs, urine output, and hemodynamic measurements to avoid pulmonary edema associated with fluid overload.
- Confirm the diagnosis with a calibrated thermometer to measure high temperature.
- Antipyretics have no role in the management of patients suffering from heat stroke.
- Stop cooling at 39.5 °C (103 °F) to avoid iatrogenic hypothermia.
- *Cooling measures:* The biggest predictor of outcome is the degree and duration of hyperthermia, time to initiation of cooling measures, and number of organ systems affected.
- External cooling techniques are easier to implement, effective, well-tolerated, and include the following:
  - Evaporative cooling can be accelerated by removing clothing and using a fan in conjunction with misting the skin with tepid water or applying a single-layered wet sheet to bare skin. These methods need a lot of repetition at frequent intervals to maintain their efficacy.
  - Conductive cooling—direct application of sources such as a hypothermic blanket, ice bath, or ice packs to neck, axillae, and groins. Ice packs are effective but poorly tolerated by the awake patient. Avoid vasoconstriction and shivering as vasoconstriction impedes heat loss and shivering generates heat. Shivering may be suppressed with IV diazepam (5 mg) or lorazepam (1–2 mg).
  - Convective techniques include the removal of clothing and the use of fans and air conditioners.
  - *Internal cooling techniques* such as gastric or rectal lavage, thoracic lavage, peritoneal lavage with ice-cold water, and extracorporeal blood cooling are

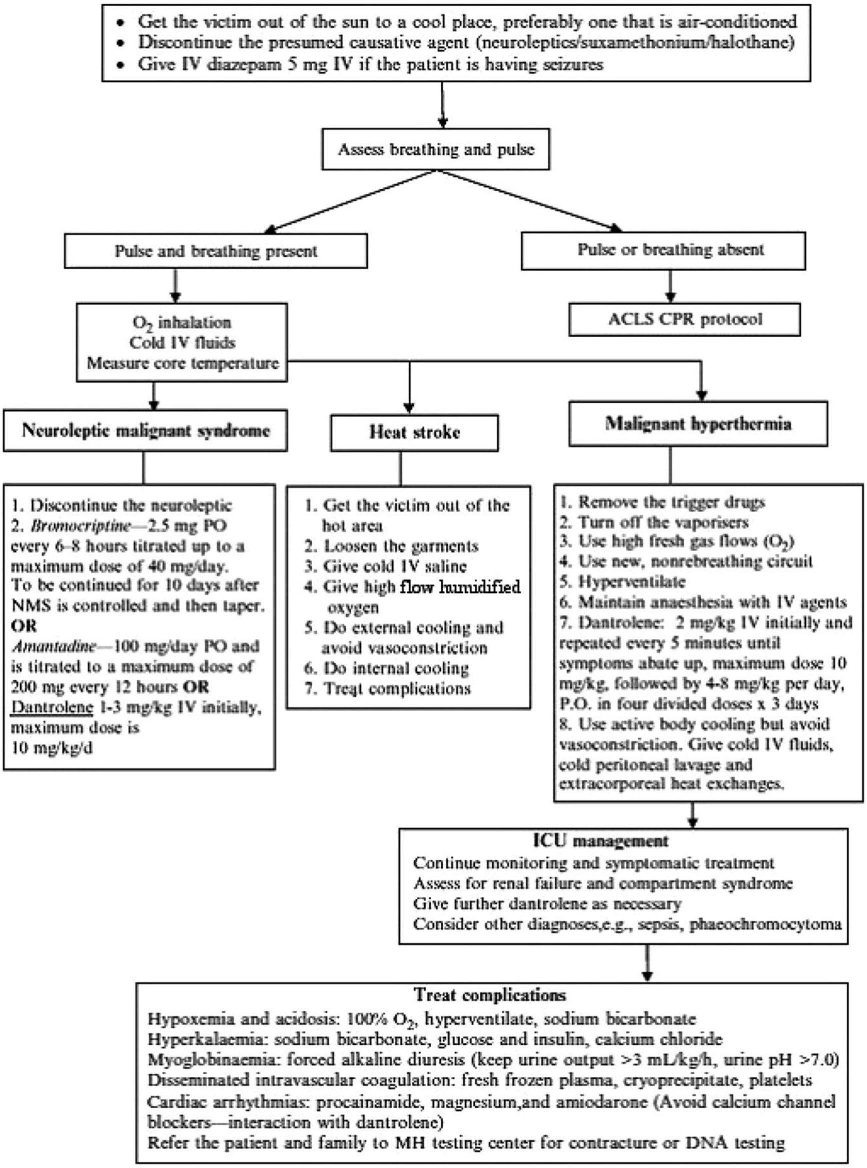
  effective, but they are difficult to manage and are associated with complications. Cold peritoneal lavage results in rapid cooling but is an invasive technique contraindicated in pregnant patients or those with previous abdominal surgery.
  - Devices utilized in TTM, i.e., invasive cooling catheters and noninvasive adhesive pads circulating chilled water may also be utilized in heat-related illnesses.
  - Cold humidified O_2 and cold IV fluids are useful adjuncts.

Step 5: Specific Management: Malignant Hyperthermia and Neuroleptic Malignant Syndrome

- Dantrolene, a nonspecific skeletal muscle relaxant, is the mainstay of treatment. It acts by blocking the release of calcium from the sarcoplasmic reticulum, thereby decreasing the myoplasmic concentration of free calcium and diminishing the myocyte hypermetabolism causing the symptoms. The prognosis is dependent upon the earlier administration of the drug.
- There is an associated risk of hepatotoxicity with dantrolene (see Fig. 35.1 for details).

Step 6: Management of Complications

- *Rhabdomyolysis.*
  - Expand the intravascular volume with normal saline. The initial rate of fluid administration should be 1–2 L/h and then titrate to urine output of 3 ml/kg/h and alkalinization (pH 7.5–8.0) to prevent precipitation of myoglobin in the renal tubules, metabolic acidosis, and hyperkalemia.
  - Avoid volume overload in patients who have developed AKI.
  - The goal is to prevent myoglobin-induced renal injury by promoting renal blood flow leading to diuresis. Monitor serum electrolytes to prevent life-threatening arrhythmias.
  - Urinary alkalinization: In patients where diuresis has been achieved with volume administration, intravenous soda bicarbonate infusion may be given. It should be discontinued if urine pH does not rise above 6.5 after 3–4 h. Avoid soda bicarbonate in patients with hypocalcemia and volume overload.
  - Loop diuretics or Mannitol have not been shown to be effective.
- *Hypotension*: To sustain organ perfusion, hypotension refractory to fluid optimization should be managed by vasopressors, to maintain MAP >65 mm Hg.
- *Seizures* should be monitored with EEG and managed with IV benzodiazepines and levetiracetam.
- *Multiorgan failure*: Give supportive therapy until organ function recovers.



- Get the victim out of the sun to a cool place, preferably one that is air-conditioned
- Discontinue the presumed causative agent (neuroleptics/suxamethonium/halothane)
- Give IV diazepam 5 mg IV if the patient is having seizures

Assess breathing and pulse

Pulse and breathing present

O_2 inhalation
Cold IV fluids
Measure core temperature

Pulse or breathing absent

ACLS CPR protocol

Neuroleptic malignant syndrome

1. Discontinue the neuroleptic
2. *Bromocriptine*—2.5 mg PO every 6–8 hours titrated up to a maximum dose of 40 mg/day. To be continued for 10 days after NMS is controlled and then taper.

OR

Amantadine—100 mg/day PO and is titrated to a maximum dose of 200 mg every 12 hours **OR** Dantrolene 1-3 mg/kg IV initially, maximum dose is 10 mg/kg/d

Heat stroke

1. Get the victim out of the hot area
2. Loosen the garments
3. Give cold IV saline
4. Give high flow humidified oxygen
5. Do external cooling and avoid vasoconstriction
6. Do internal cooling
7. Treat complications

Malignant hyperthermia

1. Remove the trigger drugs
2. Turn off the vaporisers
3. Use high fresh gas flows (O_2)
4. Use new, nonrebreathing circuit
5. Hyperventilate
6. Maintain anaesthesia with IV agents
7. Dantrolene: 2 mg/kg IV initially and repeated every 5 minutes until symptoms abate up, maximum dose 10 mg/kg, followed by 4-8 mg/kg per day, P.O. in four divided doses x 3 days
8. Use active body cooling but avoid vasoconstriction. Give cold IV fluids, cold peritoneal lavage and extracorporeal heat exchanges.

ICU management

Continue monitoring and symptomatic treatment
Assess for renal failure and compartment syndrome
Give further dantrolene as necessary
Consider other diagnoses,e.g., sepsis, phaeochromocytoma

Treat complications

Hypoxemia and acidosis: 100% O_2, hyperventilate, sodium bicarbonate
Hyperkalaemia: sodium bicarbonate, glucose and insulin, calcium chloride
Myoglobinaemia: forced alkaline diuresis (keep urine output >3 mL/kg/h, urine pH >7.0)
Disseminated intravascular coagulation: fresh frozen plasma, cryoprecipitate, platelets
Cardiac arrhythmias: procainamide, magnesium,and amiodarone (Avoid calcium channel blockers—interaction with dantrolene)
Refer the patient and family to MH testing center for contracture or DNA testing

Fig. 35.1 Management of hyperthermia

Step 7: Prevention

- Hyperthermia, caused by physical exertion or a hot environment, can be prevented by maintaining hydration and taking frequent rest breaks.
- Genetic testing can be used to evaluate individual susceptibility in patients belonging to families with a history of malignant hyperthermia.

Hypothermia

An 82-year-old female was found unresponsive in her backyard. She had a history of Alzheimer's disease and hypothyroidism since the last 10 years for which she was prescribed aspirin, olanzapine, and levothyroxine. On examination, clinical findings included cold peripheries, severe bradycardia, feeble pulse, and a Glasgow Coma Scale of 3.

Hypothermia is defined as a core body temperature below 35° C. Accurate diagnosis depends on the use of a digital or low-reading glass thermometer. It is ideally measured by using esophageal, rectal, or bladder probes. Tympanic thermometers may reflect the carotid artery temperature and can be reasonably reliable under ideal conditions.

Step 1: Initiate Resuscitation

- On admission, a primary survey (airway, breathing, circulation, disability, and exposure (ABCDE)) is conducted and resuscitation is initiated as per Chap. 24.
- Remove wet clothing, and replace it with a warm, dry sheet/blanket.
- Severely hypothermic patients are intubated gently and ventilated with warmed humidified O_2 while monitoring for cardiac dysrhythmias.
- Pulse oximetry probes placed on ears or forehead may be more accurate than on fingers.
- Perfusion should be checked ideally by continuous wave doppler of a central artery for a full minute.
- In patients without perfusion who have an organized rhythm on a cardiac monitor or cardiac contractions seen on an echocardiogram, withhold chest compression.
- CPR should be started for asystole and pulseless electrical activity after rewarming.
- In the event of ventricular fibrillation, attempt defibrillation up to three times with DC shock (200 J) and initiate CPR.
- In patients with a core temperature <30 °C, ACLS medications like epinephrine or amiodarone should not be administered.

- If the patient is found in unfavorable terrain, a mechanical device may be used for CPR. In its absence, continuous high-quality CPR should be performed if the temperature is ≥28 °C. CPR can be performed intermittently at every 5 min, alternated with ≤5 min without CPR (if temp <28 °C) and ≤10 min without CPR (if temp <20 °C) during evacuation.
- CPR is continued until the temp is above 32 °C at which point renewed attempts at defibrillation may be attempted.
- Neuroprotective effects of hypothermia may allow recovery even after prolonged arrest.
- Start an IV line and infuse warm normal saline (40–42 °C).

Step 2: Diagnose type and Severity of Hypothermia

Primary (Accidental Hypothermia)

- Normal thermoregulation.
- Overwhelming cold exposure.

Secondary

- Abnormal thermogenesis
- Other causes include hypothyroidism, hypothalamic abnormalities, burns, sepsis, ethanol abuse, sedative-hypnotic, and oral hypoglycemics.

Investigations:

- Complete hemogram, serum glucose, serum electrolytes, PT, APTT, fibrinogen, lactate, creatinine kinase, troponin, thyroid-stimulating hormone, and serum cortisol
- Toxicology screen

Symptoms increase with the severity of hypothermia as shown in Table 35.1.

- Severe hypothermia can be further divided into stage III (23–24 °C, unconscious), stage IV (24–13.7 °C, apparent death), and stage V (<13.7 °C, death due to irreversible hypothermia).
- ECG may show Osborn (J) waves especially when the core temperature is <33 °C (Fig. 35.2).

Table 35.1 Severity and symptoms of hypothermia

I	Mild (32–35 °C)	Shivering, amnesia/dysarthria, loss of coordination, tachycardia, tachypnoea, normotensive, and cold diuresis
II	Moderate (28–32 °C)	Shivering is absent, hypotension, bradycardia/atrial fibrillation, bradypnea, cognitive decline, lethargy, and paradoxical undressing
III	Severe (<28 °C)	Fixed, dilated pupils, absent oculocephalic reflexes, severe hypotension, bradycardia, ventricular fibrillation, asystole, apnea, areflexia, flat EEG, coma

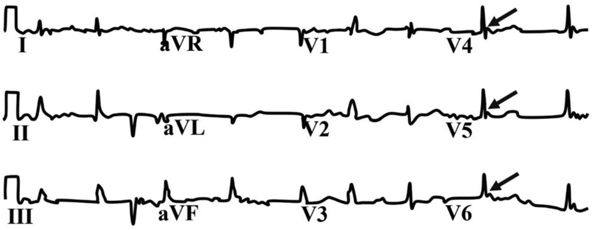


Fig. 35.2 Osborn (J) waves (marked with arrows)

- It is a positive deflection seen at the junction of QRS and ST segment in leads V3–V6 and its amplitude is proportional to the degree of hypothermia.
- In hypothermia, ECG changes induced by hyperkalemia may be obscured.

Step 3: Manage Hypothermia

Mortality in moderate to severe hypothermia approaches 50% despite best care, hence treatment should begin without delay. The patient should be handled gently, as movements may precipitate lethal arrhythmias. The patient may be warmed using the following rewarming methods**:** passive, active external, and active internal.

- *Passive rewarming*: It allows endogenous heat production to increase the core temperature, provided the patient's heat-conserving mechanisms are intact (i.e., shivering,). It also includes decreasing heat loss by removing from a cold environment, removing wet clothes, and providing a blanket. Passive warming increases body temperature by 0.5–2.0 °C/h and is the method of choice for mild hypothermia and an adjunct for moderate hypothermia.
- *Active external rewarming*: It involves transferring exogenous heat to the patient by heating blankets (fluid filled), air blankets, radiant warmers, immersion in a hot bath (44–45 °C), hot water bottles, and heating pads. The rewarming rate is 1–2.5 °C/h. The trunk should be rewarmed before the extremities to prevent the paradoxical after-drop phenomenon, which shunts the warm blood to the periphery, further dropping the core body temperature.
- *Active internal warming*: It is done by warm IV fluids (40–42 °C), warm and humidified oxygen, and/or gastric/esophageal/bladder/rectal/ peritoneal or pleural lavage.
- Intermittent hemodialysis (IHD), continuous arteriovenous rewarming, cardiopulmonary bypass, and extracorporeal membrane oxygenation (ECMO) are alternative methods. IHD can raise the core temperature by 2–3 °C/h.
- Arteriovenous (AV) rewarming raises the temperature by 4–5 °C/h.

- Cardiopulmonary bypass (CPB) and veno-arterial extracorporeal life support are methods of choice used for rewarming patients with cardiac arrest and severe hypothermia and hyperkalemia. CPB and ECMO also improve oxygenation and circulatory support while raising the temperature (up to 7 °C/h), but require anticoagulation, which worsens bleeding diathesis.
- ECMO is useful in patients with core temp. <30 °C. This strategy ensures adequate circulation, oxygenation, and ventilation while the core body temperature is increased slowly. If cardiopulmonary bypass facilities are not available, a combination of invasive rewarming methods may be used. Once spontaneous circulation is returned, passive or active external rewarming methods can be used. BLS should be continued till the core temperature reaches 30 °C. Cardioactive drugs and further defibrillation should be withheld until this temperature is reached.
- Atrial arrhythmias should be monitored without intervention, as the ventricular response is slow, and unless pre-existent, most will convert to sinus rhythm spontaneously during rewarming. But pre-existing ventricular ectopy may be suppressed by hypothermia and can reappear during rewarming. Bretylium tosylate, a class III ventricular anti-arrhythmic, is the drug of choice.
- Patients in asystole may need rewarming to 35 °C before cardiac rhythm is restored.
- Electrolytes, glucose, and thyroid profile should be assessed and corrected if required.
- For patients who fail to rewarm properly after aggressive rewarming procedures, treat empirically for sepsis, adrenocortical insufficiency, and hypothyroidism.

Stepwise management of hypothermia is shown in Fig. 35.3.

If core body temperature does not respond to warming efforts, underlying infection or endocrine derangements must be considered. Treatment with a broad-spectrum antibiotic and glucocorticoid/levothyroxine may be instituted empirically.

Step 4: Manage Associated Complications

Like bleeding diathesis, frostbite, dry gangrene, wet gangrene, acute kidney injury, infection, rhabdomyolysis, pulmonary edema, and pancreatitis.

Various complications are associated with rewarming also, which range from electrolyte abnormalities (hyperkalemia, hypophosphatemia, hypomagnesemia, and hypocalcemia), impaired glucose metabolism, platelet dysfunction to systemic inflammation, cardiac arrhythmias, and Takotsubo cardiomyopathy.

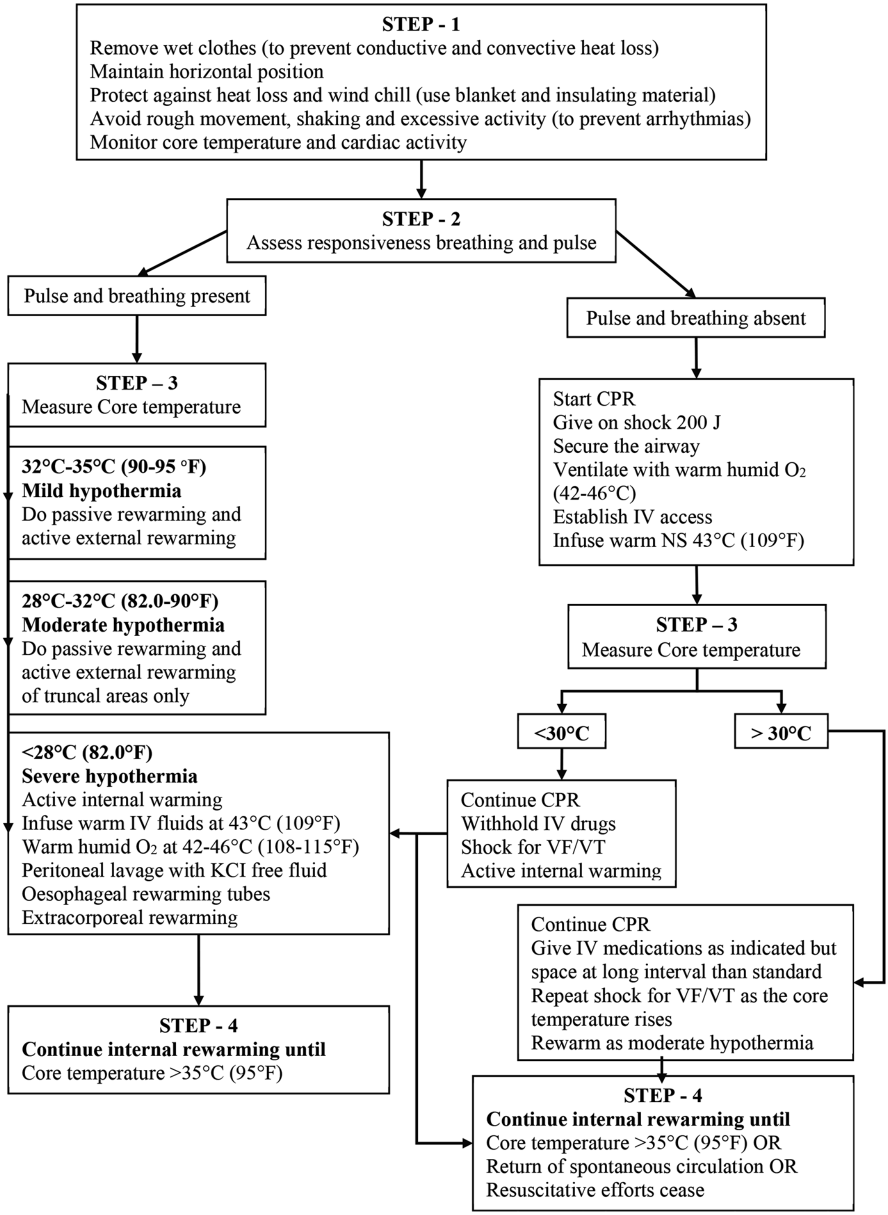

STEP - 1
Remove wet clothes (to prevent conductive and convective heat loss)
Maintain horizontal position
Protect against heat loss and wind chill (use blanket and insulating material)
Avoid rough movement, shaking and excessive activity (to prevent arrhythmias)
Monitor core temperature and cardiac activity
STEP - 2
Assess responsiveness breathing and pulse
Pulse and breathing present
Pulse and breathing absent
STEP – 3
Measure Core temperature
32°C-35°C (90-95 °F)
Mild hypothermia
Do passive rewarming and active external rewarming
28°C-32°C (82.0-90°F)
Moderate hypothermia
Do passive rewarming and active external rewarming of truncal areas only
<28°C (82.0°F)
Severe hypothermia
Active internal warming
Infuse warm IV fluids at 43°C (109°F)
Warm humid O2 at 42-46°C (108-115°F)
Peritoneal lavage with KCI free fluid
Oesophageal rewarming tubes
Extracorporeal rewarming
STEP - 4
Continue internal rewarming until
Core temperature >35°C (95°F)
Start CPR
Give on shock 200 J
Secure the airway
Ventilate with warm humid O2 (42-46°C)
Establish IV access
Infuse warm NS 43°C (109°F)
STEP – 3
Measure Core temperature
<30°C
> 30°C
Continue CPR
Withhold IV drugs
Shock for VF/VT
Active internal warming
Continue CPR
Give IV medications as indicated but space at long interval than standard
Repeat shock for VF/VT as the core temperature rises
Rewarm as moderate hypothermia
STEP - 4
Continue internal rewarming until
Core temperature >35°C (95°F) OR
Return of spontaneous circulation OR
Resuscitative efforts cease

Fig. 35.3 Stepwise management of hypothermia

Disaster Management

Case Vignette

The emergency department of a tertiary care hospital received five workers from a chemical factory with complaints of skin burns and severe respiratory distress. The patients presented with irritability, lacrimation, salivation, and tachypnoea. Eyewitnesses reported a loud blast in the boiler and a strong pungent irritable smell in the vicinity, from where these patients were rescued.

Disaster is defined by WHO as a serious disruption of the functioning of a community or a society at any scale due to hazardous events interacting with conditions of exposure, vulnerability, and capacity, leading to one or more of the following: human, material, economic, and environmental losses and impacts.

A disaster may either be natural (earthquake, landslide, cyclone, floods, avalanche, etc.) or man-made (radiation, chemical, biological, industrial accidents, oil spills, terrorist attacks, war, explosions, etc.). The primary management in a disaster is focused on limiting the critical mortality rate and therefore, a basic management protocol is implemented. National Disaster Management Authority, India, and similar agencies worldwide provide the essential resources for the management of these disasters with a dedicated helpline for guidance.

Immediately upon reporting, the hospital's disaster management plan is activated and communication with regional and/ or national authorities is established for reporting and guidance of the disaster-specific protocol. A rapid response team consisting of different specialists and paramedical staff is activated.

Hospital preparedness is of utmost importance for the management of disaster-related scenarios, which requires periodic training and education of hospital personnel, mock drills, interhospital communication, and partnership for setting up emergency response. The disaster management protocol can be broadly categorized into three steps: decontamination, triage, and emergency management.

Step 1: Decontamination

Patients encountering natural disasters rarely require decontamination, but it is an essential component for management in man-made disasters. After initial triage and referral to the hospital, patients are shifted to a Decontamination Zone (DCZ). DCZ has separate entrances, ventilation arrangements (air-locked rooms fitted with adsorbent/HEPA filters and positive air circulation), and contaminated water collection facilities. Attending staff should wear personal protective gear. The patient is completely exposed for assessment and personal belongings are separately sealed in packages (except for critical devices such as hearing aids). Warm water and soap are used to gently scrub the patient and to avoid skin breakdown and wound contamination. Wounds are carefully cleaned and irrigated with water or saline.

Table 35.2 START protocol

Color code	Category	Signs and symptoms	Interpretation
Red	Immediate	Not able to walk and: Radial pulse absent/ capillary refill>2 s OR spontaneous breathing: Absent or RR > 30/min OR mental status: Not oriented	Patients requiring immediate life-saving interventions. Requires medical attention within minutes for survival (60 min)
Yellow	Delayed	Not able to walk and: Radial pulse present/ capillary refill <2 s OR RR < 30/min, spontaneous breathing present OR Mental status: oriented/following commands	Patients who do not need immediate intervention and can wait for a few hours without deterioration
Green	Minor	Walking, wounded, minor injuries	Patients requiring only minimal medical care Unlikely to deteriorate over days
Black	Deceased	Not able to walk and: Apnea present	Victim unlikely to survive. Provide palliative care and pain relief

Step 2: Triage

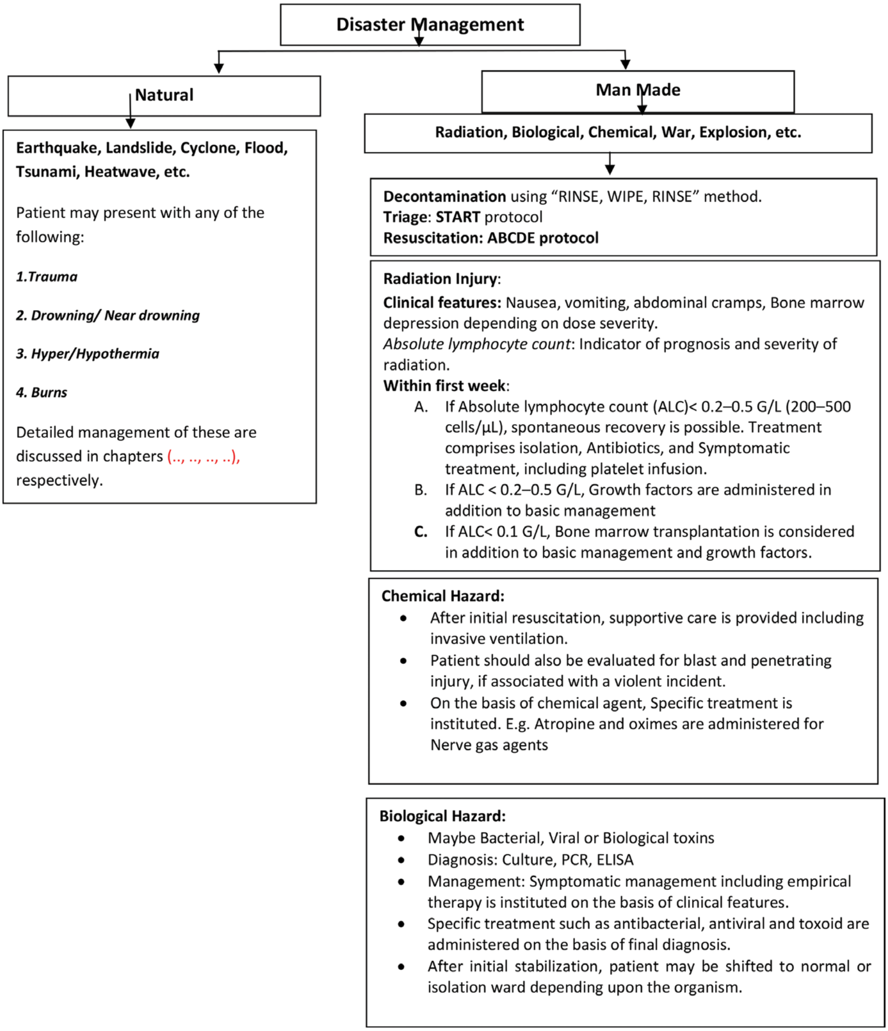
Triage includes rapidly identifying the patients and assigning priorities for care based on the severity of injury and resource availability. On arrival in the ED, a patient is properly labeled into the four categories described in Table 35.2 on the basis of the START protocol.

Record keeping, labeling, and identification are of utmost importance.

Step 3: Emergency Management

- After triage, the patient is provided definitive care and management on the basis of their category and clinical presentation. Point-of care investigations such as hemogram, arterial blood gas analysis, and extended FAST help in the quicker identification of ailment and rapid correction.
- Patients in natural disasters may present with the features of trauma, drowning, hypothermia, and burns as the case may be. Detailed management of these disorders has been mentioned in Chaps. 18, 19, 24, Vol. I.
- Critically injured patients are best managed in the resuscitation zone, where cardiac and trauma emergencies are managed, as per the previously discussed protocol elsewhere in the book.

- Patients are further provided surgical intervention that may range from damage control to definitive surgeries depending on the level of injuries. This may include splinting of fractures, tetanus immunization, primary wound closure, or debridement. The minor ailments are dealt with least priority. Post-disaster, many patients may develop mental health issues (anxiety, depression, nightmares, or worsening of pre-existing psychiatric conditions) that will require prolonged treatments.
- A strict infection control policy is a must while managing any kind of victims of disaster. A brief outline of the management of disaster is described in Fig. 35.4.



Earthquake, Landslide, Cyclone, Flood, Tsunami, Heatwave, etc.

Patient may present with any of the following:

1.Trauma

2. Drowning/ Near drowning

3. Hyper/Hypothermia

4. Burns

Detailed management of these are discussed in chapters (.., .., .., ..), respectively.

Radiation, Biological, Chemical, War, Explosion, etc.

Decontamination using "RINSE, WIPE, RINSE" method.
Triage: **START** protocol
Resuscitation: ABCDE protocol

Radiation Injury:

Clinical features: Nausea, vomiting, abdominal cramps, Bone marrow depression depending on dose severity.
Absolute lymphocyte count: Indicator of prognosis and severity of radiation.
Within first week:

A. If Absolute lymphocyte count (ALC)< 0.2–0.5 G/L (200–500 cells/μL), spontaneous recovery is possible. Treatment comprises isolation, Antibiotics, and Symptomatic treatment, including platelet infusion.
B. If ALC < 0.2–0.5 G/L, Growth factors are administered in addition to basic management
C. If ALC< 0.1 G/L, Bone marrow transplantation is considered in addition to basic management and growth factors.

Chemical Hazard:

- After initial resuscitation, supportive care is provided including invasive ventilation.
- Patient should also be evaluated for blast and penetrating injury, if associated with a violent incident.
- On the basis of chemical agent, Specific treatment is instituted. E.g. Atropine and oximes are administered for Nerve gas agents

Biological Hazard:

- Maybe Bacterial, Viral or Biological toxins
- Diagnosis: Culture, PCR, ELISA
- Management: Symptomatic management including empirical therapy is instituted on the basis of clinical features.
- Specific treatment such as antibacterial, antiviral and toxoid are administered on the basis of final diagnosis.
- After initial stabilization, patient may be shifted to normal or isolation ward depending upon the organism.

Fig. 35.4 Overview of disaster management

Suggested Reading

Douma MJ, Aves T, Allan KS, Bendall JC, Berry DC, Chang WT, Epstein J, Hood N, Singletary EM, Zideman D, Lin S. First Aid Task Force of the International Liaison Committee on Resuscitation. First aid cooling techniques for heat stroke and exertional hyperthermia: A systematic review and meta-analysis. Resuscitation. 2020:148173–90. https://doi.org/10.1016/j.resuscitation.2020.01.007. *Water immersion techniques, using water between 1 and 17°C, have been shown to lower core body temperatures more effectively than passive cooling in hyperthermic adults. The evidence indicates that water immersion can rapidly reduce core body temperature in settings where it is practical*.

Wasserman DD, Thurman J, Healy M. EMS methods to cool a patient in the field. 2023 Jul 3. In: StatPearls [internet]. Treasure Island (FL): StatPearls Publishing; 2024

Duong H, Patel G. Hypothermia. [Updated 2024 Jan 19]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024. Available from: https://www.ncbi.nlm.nih.gov/books/NBK545239/

Benson M, Koenig KL, Schultz CH. Disaster triage: START, then SAVE–a new method of dynamic triage for victims of a catastrophic earthquake. Prehosp Disaster Med. 1996;11(2):117–24. https://doi.org/10.1017/s1049023x0004276x. *The MDR-SAVE methodology is the first systematic attempt to use triage as a tool to maximize patient benefit in the immediate aftermath of a catastrophic disaster.*

Government of India. National Disaster Management Authority [Internet]. New Delhi (India). [Reviewed 2022; cited 2024 sep 24]. Available from: ndma.gov.in

Scoring Systems

36

Jigeeshu V. Divatia and Mihika Divatia

Severity of Illness Scoring Systems

A 60-year-old male patient with cirrhosis of the liver and portal hypertension was admitted to the hospital with pneumonia. He developed septic shock and became encephalopathic and anuric. The family wanted to know the chances of survival. Can a scoring system be used to predict the chances of survival?

The annual mortality in the ICU patients of hospital A is 5% and of hospital B is 15%. Can it be concluded that the ICU patients of Hospital B are poorly managed compared to those of Hospital A?

Performance measures of ICU care are usually subjective and difficult to compare. An objective measure of the structure, processes, and outcome by prognosticating in a cohort of ICU patients makes it more meaningful and easier to compare. This also helps in the rational allocation of resources. A severity scoring system also helps in controlling risk factors in intervention and control groups in clinical trials.

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Step 1: Understand the Type of Scoring Systems Used in the ICU Population

- General risk-prognostication scores (severity of illness scores)
  - Acute physiology and chronic health evaluation (APACHE II, III, and IV)
  - Simplified acute physiology score (SAPS II and III)
  - Mortality prediction model (MPM II0 and MPM II24)
- Disease and organ-specific risk-prognostication scores
  - Ranson's score for acute pancreatitis
  - RIFLE and AKIN classification for acute kidney injury
  - Trauma scores
  - Glasgow coma score
  - KILLIP—heart failure
  - CURB-65—pneumonia
  - CAM-ICU—delirium
- Organ dysfunction score—sequential organ failure assessment (SOFA)
- Nursing workload measurement—therapeutic intensity scoring systems (TISS)
- Population-specific—pediatrics—APGAR score
- Postoperative—PRISM

Step 2: Understand General ICU Scoring Systems

- All scoring systems are developed from large databases of ICU patients called the derivation cohort.
- Statistical modeling is used to determine the variables that are likely to impact survival.
- A summary score is derived from these variables, and the predicted mortality is calculated using predictive equations, which is validated in another set of ICU patients called the validation cohort.
- The performance of the scoring system depends on the size and case mix of patients in the reference database and the methodology used to assign weights to different elements of the scoring system.
- APACHE II and SAPS II scoring systems were derived from datasets of patients in North American and European ICUs in the mid-1980s and early 1990s.
- The APACHE II scoring system assigns points to age, acute physiological observations based on the worst values in the first 24 h after admission for 12 variables, and specified preexisting chronic diseases. It also requires the selection of a single diagnostic category for each patient. The predicted mortality is based on the APACHE II score and the diagnostic category (Table 36.1).
- The SAPS scoring system does not require ICU admission diagnosis to calculate the score.
- Both APACHE II and SAPS II did not account for lead-time bias (i.e., the time lag between the onset of critical illness and admission to the ICU).

Table 36.1 The APACHE II scoring system

	High abnormal range					Low abnormal range			
Physical variable	+4	+3	+2	+1	0	+1	+2	+3	+4
Temperature—rectal (°C)	>41	39–40.9		38.5–38.9	36–38.4	34–35.9	32–33.9	30–31.9	<29. 9
Mean arterial pressure (mmHg)	≥160	130–159	110–129		70–109		50–69		≤49
Heart rate (ventricular response)	≥180	140–179	110–139		70–109		55–69	40–54	≤39
Respiratory rate (nonventilated or ventilated)	≥50	35–49		25–34	12–24	10–11	6–9		≤5
Oxygenation: A-aDO$_2$or PaO$_2$(mmHg)									
(a) FiO$_2$ ≥ 0.5 record A-aDO$_2$	≥500	350–499	200–349		<200				PO$_2$
(b) FiO$_2$ < 0.5 record PaO$_2$					PO$_2$ > 70	PO$_2$61–70		PO$_2$55–60	PO$_2$ < 55
Arterial pH	≥7.7	7.6–7.69		7.5–7.59	7.33–7.49		7.25–7.32	7.15–7.24	<7.15
Serum sodium (mMol/L)	≥180	160–179	155–159	150–154	130–149		120–129	111–119	≤110
Serum potassium (mMol/L)	≥7	6–6.9		5.5–5.9	3.5–5.4	3–3.4	2.5–2.9		<2.5
Serum creatinine (mg/100 mL) (double-point score for acute renal failure)	≥3.5	2–3.4	1.5–1.9		0.6–1.4		<0.6		
Hematocrit (%)	≥60		50–59.9	46–49.9	30–45.9		20–29.9		<20
White blood count (total/mm^3) (in 1000 s)	≥40		20–39.9	15–19.9	3–14.9		1–2.9		<1

(continued)

Table 36.1 (continued)

	High abnormal range					Low abnormal range			
Physical variable	+4	+3	+2	+1	0	+1	+2	+3	+4
Glasgow coma score (GCS) score = 15 minus actual GCS									
[A] Total acute physiology score (APS), sum of the 12 individual variable points									
Serum HCO_3 (venous mMol/L) (not preferred, use if no ABGs)	≥52	41–51.9		32–40.9	22–31.9		16–21.9	15–17.9	≤15
[B] Age points									
Assign points to age as follows:									
Age (years)					Points				
≤44					0				
45–54					2				
55–64					3				
65–74					5				
≥75					6				
[C] Chronic health points									
If the patient has a history of severe organ system insufficiency or is immunocompromised, assign points as follows:									
(a) For nonoperative or emergency postoperative patients, 5 points									
(b) For elective postoperative patients, 2 points									
Definitions									
Organ insufficiency or immunocompromised state must have been evident prior to this hospital admission and conform to the following criteria:									
Liver: Biopsy-proven cirrhosis and documented portal hypertension, episodes of past upper GI bleeding attributed to portal hypertension, or prior episodes of hepatic failure/encephalopathy/coma									
Cardiovascular: New York Heart Association Class IV									
Respiratory: Chronic restrictive, obstructive, or vascular disease resulting in severe exercise restriction (i.e., unable to climb stairs or perform household duties, or documented chronic hypoxia, hypercapnia, secondary polycythemia, severe pulmonary hypertension (>40 mmHg), or respirator dependency)									

Renal: Receiving chronic dialysis
Immunocompromised: The patient has received therapy that suppresses resistance to infection (e.g., immunosuppression, chemotherapy, radiation, long-term or recent high-dose steroids), or has a disease that is sufficiently advanced to suppress resistance to infection (e.g., leukemia, lymphoma, and AIDS)
APACHE II score
Sum of **[A]**+ **[B]**+ **[C]**
A ASP Points____________________
B Age points____________________
C Chronic health points____________
Total APACHE II___________________

- APACHE III was developed as a further refinement of APACHE II, but its mortality prediction equations are not in the public domain.
- The APACHE IV system (2006) is based on 110,558 patients in 104 North American intensive care and coronary care units between 2003 and 2004. It uses 129 variables derived from the worst values from the initial 24 h of ICU admission. It has equations to predict both hospital mortality as well as length of ICU stay.
- SAPS III, published in 2005, was based on 16,789 patients aged 16 years or more from more than 300 ICUs in 35 countries across all continents. Three subscores—namely, patient characteristics before admission (5 variables), circumstances of admission (5 variables), and acute physiology (10 variables)—are summed up to produce the SAPS III score. A diagnostic category is essential for estimating mortality.
- Both APACHE IV and SAPS III account for lead-time bias but have not been tested and validated as extensively as APACHE II and SAPS II.
- MPM II0, published in 1985, was the first general severity model to assess the risk of death based on parameters assessed at ICU admission. Prediction models for assessment at admission and after 24 h (MPM II24) were developed originally. The models consist mainly of dichotomous variables. Data entry is the easiest for all the MPM systems as they have used only clinical variables and bedside physiological parameters, and no laboratory data.
- All ICU scoring systems predict the likelihood of hospital mortality for a population of patients admitted to the ICU.
- Some scoring system (e.g., APACHE IV also predicts the ICU length of stay).

Step 3: Understand the Organ Failure Scoring System

- The SOFA score is a descriptive score that uses routinely collected data for the calculation of a score of 0–4 for each organ, the higher number meaning more severe failure (Table 36.2).
- Daily scoring enables monitoring of the progress of organ dysfunction or failure.
- There are no equations to estimate mortality. However, high initial SOFA scores and worsening of SOFA scores over time correlate with increased mortality.
- The logistic organ dysfunction system (LODS) was developed for the evaluation of organ dysfunction on the first day of the ICU.
- It provides the probability of hospital mortality, distinguishing it from merely descriptive models such as SOFA.
- The SOFA score has recently been incorporated into the definition of sepsis.
- Sepsis is defined as life-threatening organ dysfunction caused by a dysregulated host response to infection.
- Organ dysfunction can be identified as an acute change in total SOFA score ≥2 points consequent to the infection. The baseline SOFA score can be assumed to be zero in patients not known to have preexisting organ dysfunction.

Table 36.2 The SOFA score

SOFA score					
	0	1	2	3	4
Respiration PaO_2/FiO_2	>400	≤400	≤300	≤200 with respiratory support	≤100 with respiratory support
Coagulation Platelets ($10^3/mm^3$)	>150	≤150	≤100	≤50	≤20
Liver					
Bilirubin (mg/dL)	1.2	1.2–1.9	2.0–5.9	6.0–11.9	>12.0
(μmol/L)	<20	20–32	33–101	102–204	>204
Cardiovascular					
Hypotension	No hypotension	MAP <70 mmHg	Dopamine ≤5 or dobutamine (any dose)[a]	Dopamine ≥5 or epi 0.1 (or norepi ≤0.1)[a]	Dopamine >15 or epi 0.1 (or norepi ≥0.1)[a]
Central nervous system					
Glasgow coma score	15	13–14	10–12	6–9	<6
Renal					
Creatinine (mg/dL)	<1.2	1.2–1.9	2.0–3.4	3.5–4.9	>5.0
(μmol/L)	<110	110–170	171–299	300–400	>400
or urine output				or <500 mL/day	or <200mL/day

Epi epinephrine, *norepi* norepinephrine

[a] Adrenergic agents administered for at least 1 h (doses given are in μg/kg/min)

- A qSOFA (quick SOFA) score consisting of any two of the following parameters altered mentation, systolic blood pressure ≤100 mm Hg, and respiratory rate ≥22/min is a simple bedside score to identify adult patients with suspected infection who are likely to have poor outcomes. This score is no longer recommended for screening purposes by the Surviving Sepsis Campaign.

Step 4: Evaluate the Scoring System

- The ability of a model to distinguish between patients who survive and the patients who do not survive is termed discrimination. For example, if a scoring system predicts mortality of 90%, the discrimination is perfect if the observed mortality is 90%.
- The area under the receiver operating characteristic curve (AUC) is used to give a graphical and numerical estimate of discrimination. If AUC is 0.5, it means the system is only as good as flipping a coin, and if AUC is 1, this indicates excellent discrimination.
- Calibration of a system examines the difference between the observed and expected deaths in patients grouped into different severity of illness. For

example, a scoring system will be highly calibrated if it were accurate at mortalities of 90%, 50%, and 20%.

- This can be evaluated graphically as well as by goodness-of-fit statistics using the Hosmer–Lemeshow test. If the p-value is more than 0.05, the model provides a good fit for the data.
- The standardized mortality ratio (SMR = actual mortality/predicted mortality) also takes into account the severity of illness and evaluates risk-adjusted ICU performance.

Step 5: Understand the Limitations of the Scoring System

- None of the scoring systems are accurate enough to make predictions in individual patients and hence cannot be used to predict outcomes of individual patients.
- These scores give the probability of survival in a group of patients with comparable scores.
- For a given individual with an APACHE score with predicted mortality of 30% cannot be used to predict whether he would survive or die during ICU stay.
- Most systems require data to be collected in the first 24 h after ICU admission; hence, the severity score cannot be used to decide whether to admit a patient to the ICU.
- Erroneous conclusions can be drawn if data are not collected correctly according to the original database and definitions of the scoring system.
- The score cannot be applied to patients excluded from the original database (e.g., patients younger than 16 or 18 years and patients with burns).
- Missing data and interobserver variability can affect accuracy.
- APACHE IV poses a heavy burden for manual data entry as it scores 129 variables. This is not a problem in health systems where data is captured directly from the monitors and the electronic health record but is currently a major limitation in Indian ICUs.
- These scores may not be accurate in geographical regions, and the case-mix is significantly different from that in the original database.
- The performance of a scoring system tends to deteriorate over time, due to changes in practice, therapy, and case-mix. It often leads to overestimation of mortality.
- All the scoring systems can only predict the behavior of a group of patients that matches the patients in the original database population.
- The commonly used APACHE II and SAPS II do not account for lead-time bias, i.e., the effect of treatments offered prior to arrival in the ICU, which includes the time between the onset of critical illness and arrival in the ICU, as well as the location in which the patient was treated before transfer to the ICU.
- All the scoring systems need to be updated periodically to reflect contemporary practice and patient demographics to avoid deteriorating performance over time.

Step 6: Understand the Utility of the Scoring System

- No single scoring system has been proven to be superior to the other, though APACHE systems are reasonably accurate and are being widely used.
- Scoring systems can be updated and customized to represent current practice and case-mix in particular countries or regions.
- Scoring systems may be used to evaluate the performance of an ICU using the SMR.
  - The SMR of 1 implies that mortality in the ICU is equal to what is predicted by the system. The SMR of less than 1 indicates that ICU performance is better than predicted, while the SMR of more than 1 implies poor performance.
  - The SMR may be used to compare different ICUs or the performance of the same ICU over a period. Differences in the SMR may represent differences in case mix, differences in ICU practices between observed ICUs and the ICUs that contributed patients to the derivation dataset, or differences in quality of care.
  - The trend of SMRs can be used to evaluate ICU performance over time or to compare ICUs.
- Scoring systems have been used in clinical trials to ensure the similarity of study groups in terms of severity of illness at baseline.
- APACHE IV gives predictions for ICU mortality as well as hospital length of stay.
- TISS can be used to quantify and optimize nursing workload, staffing patterns, and costs.
- The daily SOFA score is useful for monitoring the progress of organ dysfunction. If an ICU treats a large number of patients belonging to a specific group (e.g., trauma, cancer, and coronary), specific scoring systems may be used.

Early Warning Scoring Systems

A 50-year-old patient is admitted to the medical ward for community-acquired pneumonia. He is initially “stable” but is hospitalized as he has a large lobar pneumonia and a high fever. A few hours later his vitals on the wards were temperature 39 °C, heart rate 110/min, respiratory rate 24/min, SpO2 92 on oxygen via nasal prongs, and blood pressure 100/70 mmHg. Should the level of care be escalated?

Step 1: Understand the Rationale for Using Early Warning Scores (Tables 36.3 and 36.4)

Cardiac arrest or “Code Blue” teams are common in many hospital systems. However, patients usually have deranged vital signs and clinical deterioration (commonly involving the respiratory and neurological status) several hours before presenting with a critical event. Failure to detect initial deterioration can result in delays in diagnosis

Table 36.3 Modified early warning score (MEWS)

Parameter	Score						
	3	2	1	0	1	2	3
SBP (mmHg)	≤70	71–80	81–100	100–199		≥200	
Heart rate (bmin)		≤40	41–50	51–100	101–110	111–129	≥130
Respiratory rate (bpm)		<9		9–14	15–20	21–29	≥30
Temperature (°C)		<35		35–38.4		≥38.5	
Neurological status				Alert	Reacts to voice	Reacts to pain	Unresponsive
Urine output (ml/kg/h)	Nil	<0.5					

SBP systolic blood pressure

Table 36.4 National Early Warning Score 2 (NEWS-2)

Parameter	Score						
	3	2	1	0	1	2	3
Respiratory rate (bpm)	≤8		9–11	12–20		21–24	≥25
SpO2% (scale 1)	≤91	92–93	94–95	≥96			
SpO2% (scale 2)	≤83	84–85	86–87	88–92 >93 on air	93–94 on oxygen	95–96 on oxygen	≥97 on oxygen
Air or oxygen?		Oxygen		Air			
SBP (mmHg)	≤90	91–100	101–110	111–219			≥220
Heart rate (bmin)	≤40		41–50	51–90	91–110	111–130	≥131
Temperature (°C)	≤35		35.1–36	36.1–38.0	38.1–39	≥39.1	
Neurological status				Alert			CVPU

SBP systolic blood pressure, *C* confused, *V* responds to vocal command, *P* responds to pain, *U* unresponsive

and treatment that may lead to an emergency ICU admission or death. The respiratory rate is a good indicator of a potential critical event. Early warning scores incorporate routine vital signs and clinical observations that can be done by nurses in the wards into a composite score. Escalation of care can be protocolized based on categorization by the scoring system as low risk, intermediate, or high risk of deterioration.

Step 2: Know the Common Early Warning Scores

The Royal College of Physicians of the United Kingdom adopted the NEWS in 2012, and the updated version 2 of 2017 was adopted by the National Health Service of the UK.

- Low risk (1–4) score.
- Low to intermediate risk (a maximum score in any of the individual parameter): an urgent local ward response is recommended.

- Intermediate risk (5–6 aggregated score): a critical threshold. An urgent response led by a clinician and recognizing the need to call the critical care team.
- High risk (aggregated score >7): an emergent response led by a critical care team.

Step 3: Early Warning Scores Need a Robust System for Recording, Noticing, and Responding to the Risk Level

The recording system may be manual or electronic. Based on the risk level, the relevant teams need to be notified and alerted. This process can also be digitized and automated. This must lead to an effective response by the ward nurse, resident doctor, or medical emergency team, as the case may be. The ineffective functioning of any of these components can lead to failure to rescue the deteriorating patient in time.

Step 4: Integrate EWS in the Hospital System

- With increasing numbers of sick patients in hospitals and limited numbers of intensive care and high-dependency beds, it is necessary to be able to provide ward patients with enhanced monitoring and care.
- Technological advances now allow continuous, remote monitoring of most of the EWS parameters (except the neurological assessment), facilitating patient care on the wards.
- Staff education, the development of a system of tiered response triggers, the availability of a medical emergency team that responds to abnormalities, and staff concerns early are essential parts of a clinical governance system.

The patient in the case vignette has a NEWS-2 score of >7; hence, he requires urgent review by the medical emergency team.

Suggested Reading

Vincent JL. Bruzzi de Carvalho F. Severity of illness. Semin Respir Crit Care Med. 2010;31:31–8. *This article reviews the most commonly used severity-of-illness scoring systems and discusses some of their uses and limitations.*

Vincent JL, Moreno R. Clinical review: scoring systems in the critically ill. Crit Care. 2010;14(2):207. *The different types of scores should be seen as complementary, rather than competitive and mutually exclusive. It is possible that their combined use could provide a more accurate indication of disease severity and prognosis. All these scoring systems will need to be updated with time as ICU populations change and new diagnostic, therapeutic, and prognostic techniques become available*.

Khwannimit B. Serial evaluation of the MODS, SOFA and LOD scores to predict ICU mortality in mixed critically ill patients. J Med Assoc Thai. 2008;91(9):1336–42. *Serial assessment of organ dysfunction during the ICU stay is reliable with ICU mortality. The maximum score is the best discrimination comparable with APACHE II score in predicting ICU mortality.*

Zimmerman JE, Kramer AA, McNair DS, et al. Acute physiology and chronic health evaluation (APACHE) IV: hospital mortality assessment for today's critically ill patients. Crit Care Med. 2006;34:1297–310. *APACHE IV predictions of hospital mortality have good discrimination and calibration and are useful for benchmarking performance in US ICUs. The accuracy of predictive models is dynamic and should be periodically retested. When accuracy deteriorates they should be revised and updated.*

Moreno RP, Metnitz PG, Almeida E, et al. SAPS 3 investigators. SAPS 3—from evaluation of the patient to evaluation of the intensive care unit. Part 2: development of a prognostic model for hospital mortality at ICU admission. Intensive Care Med. 2005;31:1345–55. *The SAPS III admission score is able to predict vital status at hospital discharge with use of data recorded at ICU admission. Furthermore, SAPS III conceptually dissociates evaluation of the individual patient from evaluation of the ICU and thus allows them to be assessed at their respective reference levels.*

García-Del-Valle S, Arnal-Velasco D, Molina-Mendoza R, et al. Update on early warning scores. Best Pract Res Clin Anaesthesiol. 2021;35(1):105–13. *A rapid review of early warning scores, highlighting the advantages, limitations, future role and the research agenda.*

Websites

http://www.sfar.org/article/316/scoring-systems-for-icu-and-surgical-patients. For calculation of various scores.

http://www.medcalc.be/manual/roc.php. Understand the ROC curve.

Ethical Principles in End-of-Life Care

37

Raj Kumar Mani

Case Vignette

A 70-year-old male patient was admitted with a massive intracerebral bleed to the ICU for 6 days. He was on ventilatory support, with a Glasgow Coma Score of 6. According to the treating physician and neurologist, his survival chances were poor, and even if he survived, he would be fully dependent functionally. His eldest son requested withdrawal of the ventilatory support to provide comfort measures only and transfer out of the ICU.

Recognizing terminal illness and assessing the proportionality of medical interventions are an essential part of quality critical care. The shift of treatment paradigm from cure to care may take place over a variable duration of critical illness with greater prognostic clarity and understanding between the physicians and the patient/family/surrogate. The emphasis thus shifts to avoiding disproportionate medical interventions concordant with the values and wishes of the patient through skillful communication.

Step 1: Assessment of Appropriateness of Interventions Based on Accurate Prognostication

The treating team must ensure thorough clinical assessment and accurate prognostic assessment. Uncertainties must also be recognized. Assess situations when a shift to a palliative care-only option would be appropriate. The following checklist can be useful:

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1. Catastrophic brain injury (traumatic brain injury, massive acute ischemic stroke, intracranial hemorrhage, brain infections, demyelinating diseases, septic encephalopathy) with coma (other than brain death) with poor prospects for meaningful neurological recovery
2. Critical illness on a background of irreversible severe neurological disability such as traumatic quadriplegia or end-stage muscular dystrophies
3. Critical illness on a background of chronic irreversible disorders of consciousness such as advanced dementia/minimally conscious state/permanent vegetative state.
4. Post-cardiac arrest anoxic-ischemic injury with Glasgow Motor Score M ≤ 2 and neurophysiological markers of poor prognosis >3 days after return of spontaneous circulation (ROSC) having excluded confounding factors
5. Advanced or metastatic malignancy with short median survival rates if treatment options are exhausted or declined by the patient
6. Advanced age with declining functional status and frailty or multiple co-morbidities where interventions have a low probability of success or are declined by the patient
7. Acute decompensation of chronic end-stage organ failure such as pulmonary, cardiac, renal, or hepatic with low life expectancy and no option of organ transplantation; >/= 3 hospitalizations in the last 12 months
8. Worsening multiorgan failure (e.g., SOFA >15) due to acute conditions refractory to a reasonable trial of organ support
9. Any patient who expresses a desire against aggressive care or a patient without decision-making capacity with previously executed valid Advanced Medical Directive (AMD) declining such care
10. Any other clinical scenario where the answer to the question “Would you be surprised if the patient is alive at the end of 6 months–1 year” is “yes”

Step 2: Discussion and Consensus Within the Treating Team Which May Include a Senior Nurse

- Ensure that all members of the healthcare team are on board and agree to initiate this discussion.
- The overall responsibility for the decision rests with the attending physician/intensivist of the patient, who must ensure that all members of the caregiver team including the medical and nursing staff follow the same approach.

Step 3: Early and as-Needed Multidisciplinary Family Meetings

Formal multidisciplinary family communication must start within 48–72 h after admission to build trust and ensure understanding and transparency. It also helps to address the informational and emotional needs of the family.

Step 4: Shared Decision-Making Between Physicians and Family

- Check for the existence of a valid Advance Will.
- If an Advance Will is available, ensure clear communications and decision-making with the appointed healthcare proxy. If it is unavailable, which is often the case, collaborate with the family's designated decision-makers.
- During the process of shared decision-making, ensure the application of the ethical principles:

Autonomy: This is the patient's right to be fully informed and to make a choice. The patient with a sound mind has the right to refuse any treatment even if it is deemed essential for life. If the patient does not have capacity, this right is exercised on behalf of the patient through an appointed healthcare proxy or family.

Beneficence: It is the duty of care of the physician to always work for the overall good of the patient.

Nonmaleficence: This is the physician's duty of care to prevent or mitigate any harm to the overall welfare of the patient.

Distributive justice: This denotes the duty of the physician to deal with patients in a fair and non-discriminatory manner and to allocate resources equitably.

The following principles should be followed during communication:

- Meet in a quiet room free from distractions.
- Ensure the presence of relevant family members. Identify decision-maker(s) who should be consistently present.
- A multidisciplinary treating team should participate.
- Active listening is an essential skill.
- Ensure at least 50% of conversation time to the family.
- Allow emotional reactions with empathy and patience.
- Recognize and support emotions.
- Provide adverse prognosis in small chunks so that there is time to process and assimilate information.
- Avoid jargon. Use vernacular where necessary.
- Make sure the information provided is understood.
- Use candor tactfully.
- Be transparent.
- Don't avoid queries and concerns.
- Repeat information if requested or inadequately understood.
- Leave space for uncertainties.
- Avoid focusing only on physiological information.
- Talk about the overall status, the best- and worst-case scenarios.
- If death appears foreseeable, mention it without euphemisms, doing so with sensitivity.
- Avoid terms like futile care.

Step 5: Discuss the Modalities of Forgoing Life Support: DNAR, Withholding/Non-escalation, and Withdrawal/de-Escalation Modalities

- Do not intubate/resuscitate (DNI/DNR):
- Provide aggressive ICU management, except intubation (DNI) or attempts at cardiopulmonary resuscitation (DNR).
- Do not escalate:
- Refrain from escalating some or all existing life-support modalities (intubation, inotropes, vasopressors, mechanical ventilation, dialysis, antibiotics, intravenous fluids, enteral or parenteral nutrition) in the case of clinical deterioration. This approach is based on the understanding that the patient will probably die from the underlying condition.
- Withdrawal or withholding of life support:
- All or specific life-support systems such as dialysis or ventilators may be withdrawn.
- Decision not to institute new life-support treatment.
- Ethically and legally in most jurisdictions, there is no difference between withholding and withdrawing life-support therapy.
- Reiterate that stopping interventions does not mean stopping care, but means focusing adequately on the needs of the dying patients and their families.
- Must also convey non-abandonment and that the decisions are shared between the two parties. Document all communications with signatures of family members and 3 or more physicians.
- The patient/family may change the decisions about withdrawal/withholding at any time.
- Allow enough time for family to arrive at a family consensus.
- Continue all support until conflicts are resolved.

Step 6: Ensure Legal Requirements Are Met. This May Vary in Different Countries

For Indian legal requirements and an updated flow chart, please see ISCCM-IAPC EOLC position statement 2024.

Step 7: Administer Palliative and Holistic Care

- Prioritizing patient comfort over avoidance of side effects of medication
- Stopping superfluous tests, monitoring, and therapies
- Liberalizing visitation
- Displaying cultural sensitivity
- Providing spiritual support, involving spiritual persons if necessary; allowing non-intrusive religious rituals

- Non-abandonment of the patients and families
- Therapeutic conversations. Providing emotional support through empathetic conversations and bedside presence
- Transfer to the location of choice
- Providing professional caregivers administrative support for complex decision-making

Step 8: Grief and Bereavement Support

Care for the grieving by being accessible to them immediately and later after death since post-traumatic stress disorder and complicated grief are frequent.

Step 9: Oversight and Quality Control

Establish a clinical ethics committee for EOLC decisions, comprising at least four members. The committee should oversee grievance redressal, conflict resolution, audits, and quality control. The committee may include clinicians, administrators, social workers, and clinical psychologists.

Conflict Resolution

When the family may be pursuing unrealistic demands of continuing futile care as deemed by the treating senior physician, or the physician may be seeking to impose his/her wishes on the family in contradiction to their wishes, conflicts may arise. The proposed course of action in these situations may be as follows:

- A second opinion from another physician not hitherto involved in the care of the patient.
- Multiple counseling sessions explicitly informing the family of the hopeless prognosis of the patient and the futility of continuing life support.
- If the family is intransigent, then suggest transfer to another treating team willing to continue support.
- Referral to the hospital clinical ethics committee.
- Seek a judicial review.

Suggested Reading

Mishra S, Mukhopadhyay K. End-of-life care: consensus statement by Indian academy of pediatrics. Indian Pediatr. 2017;54(10):851–9. *Consensus guideline to frame the guidelines related to EOL care issues and withdrawal or with-holding treatment in situations where outcome of continued treatment is expected to be poor in terms of ultimate survival or quality of life*.

Silveira MJ, Kim SY. Advance directives and outcomes of surrogate decision making before death. N Engl J Med. 2010;362(13):1211–8. *Patients who had prepared advance directives received* *care that was strongly associated with their preferences. These findings support the continued use of advance directives*.

Luce JM, White DB. A history of ethics and law in the intensive care unit. Crit Care Clin. 2009;25(1):221–37. *This article outlines major events in the history of ethics and law in the ICU, covering the evolution of ICUs, ethical principles, informed consent and the law, medical decision-making, cardiopulmonary resuscitation, withholding and withdrawing life-sustaining therapy, legal cases involving life support, advance directives, prognostication, and futility and the allocation of medical resources.*

Salins N, Gursahani R, Mathur R, Iyer S, Macaden S, Simha N, Mani RK. Definition of terms used in limitation of treatment and providing palliative care at end of life. Indian Council of Medical Research. Indian J Crit Care Med. 2018;22(4):249–62. *Provides updated definitions of terms employed in end-of-life care by the Indian expert task force.*

Curtis JR, Treece PD. Integrating palliative and critical care: evaluation of a quality-improvement intervention. Am J Respir Crit Care Med. 2008;178(3):269–75. *Improving family satisfaction in end-of-life care may require interventions that have more direct contact with family members*.

Gerstel E, Engelberg RA. Duration of withdrawal of life support in the intensive care unit and association with family satisfaction. Am J Respir Crit Care Med. 2008;178(8):798–804. *Withdrawal of life support is a complex process that depends on patient and family characteristics. Stuttering withdrawal is a frequent phenomenon that seems to be associated with family satisfaction. Extubation should be encouraged before death if possible*.

Mani RK, Amin PA. Limiting life-prolonging interventions and providing palliative care towards the end-of-life in Indian intensive care units. Indian J Crit Care Med. 2005;9:96–107. *A position statement by the Indian Society of Critical care Medicine for end-of-life care practices*.

Mani RK, Bhatnagar S, Butola S, Gursahani R, Mehta D, Simha S, et al. Indian Society of Critical Care Medicine and Indian Association of Palliative Care Expert Consensus and Position Statements for End-of-life and Palliative Care in the Intensive Care Unit. Indian J Crit Care Med. 2024;28(3):200–50. *The updated, comprehensive, and definitive review and expert consensus recommendations integrating the ethical, clinical, and legal components of end-of-life decision-making, especially for ICU practice in India.*

Searching Literature for Clinical Questions

38

Subhasish Nayak and Swagata Tripathy

In the rapidly evolving field of medical science, staying updated with the latest research is essential for providing evidence-based care. Whether you are a clinician, academician, researcher, or student, learning and mastering the skill of literature search is fundamental. This chapter will discuss and guide us through the essential steps and strategies for an effective literature search.

Step 1: Understanding the Importance of Literature Search

- A literature search is the foundation of evidence-based practice. It allows for identifying relevant studies, guidelines, and expert opinions that inform clinical decision-making.
- A systematic literature search ensures the care provided is based on the best available evidence. It is a crucial preliminary step in conducting research and preparing study results. When systematic, it is an effective process of identifying robust references from existing data on the topic of interest, which helps in developing evidence-based guidelines, supporting research methods, and fulfilling academic requirements, with the primary objective of formulating a research question by evaluating existing literature and identifying gaps for further study.
- By reviewing the existing research meticulously, one may avoid unnecessary duplication of effort and identify potential research topics, questions, and methodologies.

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Step 2: Defining the Research Question

- The first step in a literature search is to define the research question.
- A more precise research question will help the search strategy to be focused and ensure that one finds the most relevant literature.
- In critical care research, questions often explore intervention effectiveness, diagnostic accuracy, patient outcomes, and ethical aspects.
- It clearly articulates what we are seeking to explore.
- The research question should be planned using the PICO(T) framework:
  P—Patient/Population—Who is the patient/subject?/What is the population of interest?
  I—Intervention—What is the intervention?
  C—Comparison—Is there any comparison group?
  O—Outcome—What outcomes are we expecting?
  T—Time period—What is the time over which the intervention is measured?

Let us understand through an example—If we are interested in finding out the impact of early antibiotic administration on sepsis, the PICO(T) will be "In critically ill patients with sepsis **(P),** how does early administration of broad-spectrum antibiotics **(I)** compared to delayed antibiotic therapy **(C)** affect mortality rates **(O)** within 30 days **(T)?"**

Step 3: Identify Keywords/MESH Terms

- Use of keywords—It is crucial to break down the research question into main keywords or concepts.
- Use of MeSH terms—MeSH stands for Medical Subject Headings and is generally used in databases like PubMed/MEDLINE. MeSH terms are predefined and include synonym terms related to our topic. They help us retrieve articles categorized under specific bio-medical and health-related concepts.
- Use of keywords and medical subject headings (MeSH).
- Keywords can be searched by directly typing into the search bar. The MeSH terms are standardized terms that are used in the databases. Using both, we can capture a broad range of articles. For example, if we want articles related to sepsis, we might use keywords like "sepsis," "septic shock," and "systematic inflammatory response syndrome," along with the MeSH term "sepsis."

Step 4: Choose the Right Databases

- Selecting databases relevant to the field (e.g., PubMed, EMBASE, CINAHL, PsycINFO, Web of Science, Cochrane Library, Trial registries, etc.) (Table 38.1).

Table 38.1 List of databases and what they cover

Databases	Subject covered
PubMed	Clinical medicine, healthcare, health education, healthcare service delivery, health systems, etc.
EMBASE	Clinical medicine, drug and pharmaceutical sciences, toxicology, and medical devices
PsycINFO	Psychology, psychiatry, mental health, social and behavioral sciences
CINAHL	Nursing and allied health sciences
Web of Science	Basic Sciences, social sciences, biotechnology, arts, humanities

- Google Scholar or specific journal archives may be considered for the search.
- *PubMed* is a platform that provides resources and allows users to access MEDLINE, the National Library of Medicine database. It's a medical and biomedical literature source with access to peer-reviewed journals, clinical trials, and systematic reviews.
- *EMBASE* is a subscription-based platform from Elsevier that provides access to articles related to clinical medical sciences and biomedical science, with a greater focus on drug and pharmaceutical sciences.
- *PsycINFO* contains abstracts and papers related to Psychiatry, Psychology, and Mental health. It is also called APA PsychINFO because it has been owned by the American Psychological Association since 1967.
- *CINAHL* stands for Cumulative Index to Nursing and Allied Health Literature and is subscription-based, covering areas of nursing, health administration, and allied health sciences. Articles, book chapters, and dissertations are generally available.
- *Web of Science* is a paid platform containing abstracts, articles, conference proceedings, book chapters, and other information from the arts, humanities, engineering, sciences, social sciences, etc. It is vast and covers broad areas, yielding articles from journals with high-impact factors.
- *Google Scholar* is a platform where one can search for articles, books, abstracts, opinions, etc., in the search engine. It covers various domains from different disciplines and is primarily used for iterative searching.
- Cochrane Library: It is a paid platform for high-quality, independent evidence to inform healthcare decision-making. It includes systematic reviews, clinical trials, and other resources.
- Clinical trials.gov: It is a free platform database of privately and publicly funded clinical studies conducted around the world. It is managed by the U.S. National Library of Medicine (NLM) at the National Institutes of Health (NIH). The website provides information about clinical trials, including their purpose, who may participate, locations, and contact information.

Step 5: Develop a Search Strategy

- A well-organized search strategy combines keywords, phrases, and medical subject headings (MeSH) with limits or filters used to search a database.
- The search approach will consist of the following:
  - Keywords and Boolean operators
  - Different search phrases (suffixes, synonyms)
  - Medical Subject Headings (MeSH)
- One or more of the following might be used in the search strategy:
  - Truncation (if appropriate)
  - Phrases (if appropriate)
  - Limits (publication year, language, type of article, subject, etc.)

Step 6: Conducting Search

- Testing the search strategy along the way is very important to find relevant articles. It is excellent to get the plan reviewed by co-authors. There is always a possibility that one might have missed a concept. Hence, reviewing will help to make it robust and appropriate.
- When we design a search strategy and perform a search, it is crucial to know that each database accepts different searches. So, accordingly, we must prepare our search strategy. For example, many terms differ in EMBASE than those used in PubMed.

- *How to choose search terms*

The author can write down as many terms as possible related to the research question. One of the most important things to consider is that words can be expressed differently.

For example –

(i) Synonyms: Let us take the word “Edema”—It may be “swelling,” “Fluid retention,” “Lymphedema,” OR “Anasarca.”
(ii) Abbreviations: “CKD” OR “chronic kidney disease”
(iii) Use of suffixes: Many databases allow the search words with an asterisk (*) sign as their truncation. Through this, we can discover words with endings that are singular and plural. For example, Educat*will retrieve results related to education, educator, educators, educating, educational, etc. The word “Therapy*” will retrieve results for therapy, therapies, therapists, or therapists.

- *Development of strategy*

It is essential to remember that authors should search for the exact phrase.

Sometimes, words appear next to each other. In such cases, quotation marks, e.g., “Evidence-based”, can be used.

- *Use of Boolean terms*

The terms “AND,” “OR,” and “NOT” are widely used to refine our search results. “AND” narrows our search by combining terms, “OR” broadens by including either term, and “NOT” excludes either term.

- *AND*—We are instructing the search to retrieve only those documents that contain both words or phrases (Fig. 38.1), e.g., Road Accidents AND India.
- *OR*—We are instructing the search to yield results containing either concept, e.g., Challenges OR, barriers OR weaknesses (Fig. 38.2).
- *NOT*—This will narrow our results by eliminating words or phrases (Fig. 38.3), e.g., ARDS NOT Pediatric will include articles on ARDS by excluding pediatric cases.

Note: In the above figures, the colored portions are the yielded results.

Fig. 38.1 Results will include both terms

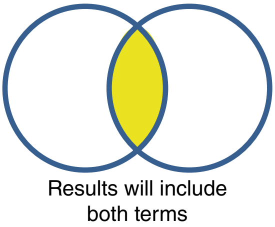

Results will include
both terms

Fig. 38.2 Results will include one or both terms

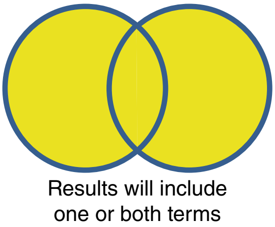
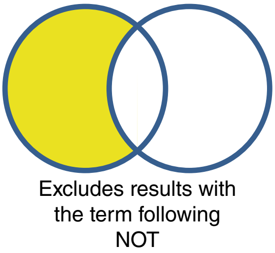

Results will include
one or both terms

Fig. 38.3 Excludes results with the term following NOT


Excludes results with
the term following
NOT

- *Use of limits and filters*

Limits and filters refine or narrow down search results, such as publication date, language, type of articles, subjects, etc.

- *Tracking of citation*

Once we have found our relevant articles, we can do citation tracking to see more articles related to the topic of interest. We may choose which articles have cited the one we are now reading from most databases. We may get more recent articles based on the subject by following the link.

Finding the most related article, in PUBMED and all related articles will retrieve all articles using similar MESH terms.

- *Gray Literature*

We should never forget to include gray literature in our search for critical care research. It includes abstracts, conference papers, therapeutic recommendations, theses, and reports. These resources can provide insightful information and the most recent discoveries that haven't yet been released in peer-reviewed publications.

Step 7: Screening and Selecting Relevant Articles

- A detailed go-through of titles and abstracts of yielded studies. This step is also called primary screening or title-abstract screening. After completing the title-abstract round, a full-text screening of selected relevant articles is performed to generate in-depth information.

For an easy way, it is best advised to download or save full texts of articles that are directly related to the research work.

Step 8: Managing References

Reference management tools are available to keep track of our sources. Software like Mendeley, EndNote, Zotero, etc., are easy to use and very helpful.

Step 9: Assessing the Quality of Evidence of Selected Articles

- It is essential to critically assess the selected articles' credibility, relevance, and quality. For quality, critical appraisal tools like JBI, MMAT, REVMAN from Cochrane, COVIDENCE, etc., can be used.

- Attention should be paid to the publication's impact factor the methodology used, and requisite and relevant information on key findings should be extracted.
- It is always advised to identify trends, gaps, and further scope of research.
- Articles are reviewed regarding biases and ranked accordingly.

Step 10: Synthesizing Evidence and Statistical Analysis

- The evidence taken from the included research must be compiled, summarized, combined, organized, and contrasted by the reviewers. The extracted data must be presented in a way that makes sense and adds something unique to the body of existing research.
- A standardized extraction form is advised for extracting data from included studies. Online platforms like Covidence and Rayyan make performing a literature review easy.

Step 11: Writing the Literature Review

- The literature review should be carefully organized into relevant subheadings/themes by plugging information into central themes or arranging it chronologically, depending on our research focus.
- A good tip during the synthesis of results is to identify and highlight key points and then show how they fit into the big picture of the research question.

In this way, the review will be logically connected, and the significance of the literature will be integrated with the study's objectives.

Step 12: Stay Updated

We must remain updated about our topic of interest, periodically seeking the presence of new publications. Email alerts, RSS feeds, and journal subscriptions are the most frequently used steps to keep updated when any new article is published.

Suggested Reading

Vincent JL, Moreno R, Takala J, Willatts S, De Mendonça A, Bruining H, et al. The SOFA (Sepsis-related Organ Failure Assessment) score to describe organ dysfunction/failure. On behalf of the Working Group on Sepsis-Related Problems of the European Society of Intensive Care Medicine. Vol. 22, Intensive care medicine. United States; 1996. p. 707–10.

Evidence-based medicine. A new approach to teaching the practice of medicine. JAMA. 1992;268(17):2420–5.

Titler M. Section II: evidence-based practice. In: Patient safety and quality: an evidence-based handbook for nurses; 2008. p. 113–32.

Grewal A, Kataria H, Dhawan I. Literature search for research planning and identification of research problem. Indian J Anaesth. 2016;60(9):635–9.

Rau JL. Searching the literature and selecting the right references. Respir Care. 2004;49(10):1242–5.

Library SM-LM. Literature Searching [Internet]. Available from: https://laneguides.stanford.edu/LitSearch/step3#:~:text=It/is/used/to/give,pre-defined/and/include/synonyms

Library CMHS. Evidence-Based Practice [Internet]. 2024. Available from: https://guides.hsl.virginia.edu/c.php?g=921177&p=6638623

Website

https://uk.sagepub.com/en-gb/eur/the-literature-review/book236719. Handbook of eHealth Evaluation: An Evidence-based Approach.

Research Methodology in Critical Care

39

Anirban Hom Choudhuri, Ajeet Bhadoria,
and Surabhi Mishra

Medical research is the only reliable way through which our insight can be focused on the best practices in medicine. The Health Insurance Portability and Accountability Act defines medical research as "a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge." Medical research is inevitable for ensuring high-quality patient care.

Critical care medicine is a unique discipline that is practiced by physicians from several primary specialties. The execution of good research is vital for intensivists to provide state-of-the-art care for patients confronting life-threatening illnesses, to improve patient outcomes and provide better utilization of ICU resources. Most importantly, good research is inevitable for advancement in the theory and practice of critical care medicine.

A Guide to the "Research Process"

The entire "research process" can be guided through an eight-step model consisting of three phases as outlined in Table 39.1.

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Table 39.1 Phases and steps of the research process

Phase 1 (Decide what to research)	Phase 2 (Plan a research)	Phase 3 (Conduct research)
Step 1: Formulate the research question	*Step 2*: Conceptualize the study design *Step 3*: Construct an instrument for data collection *Step 4*: Select a sample *Step 5*: Write a research proposal	*Step 6*: Collection of data *Step 7*: Process and display of data *Step 8*: Write a research report

Table 39.2 "FINER" approach for research question

F	Feasible	Access to an adequate number of participants Research team has the technical expertise to conduct the study Costs are reasonable and funding is available Can be completed in a reasonable time period
I	Interesting	Results of the study will be of interest to the research community
N	Novel	Provides new findings, extends or refutes previous findings
E	Ethical	Risk to participants is low/acceptable Considered ethical by peers and the IRB
R	Relevant	To improve scientific knowledge, inform clinicians and health policy, and to impact future research

Table 39.3 Format of a research question

	For example, in a comparison of outcomes after off-pump and on-pump CABG, the population consists of CAD patients, the intervention would be surgery (either on-pump or off-pump), the control would be patients on medical treatment (placebo), the outcome could be survival or death, and the time period for measuring the outcome can be chosen accordingly (e.g., in days, months, or years)

Step 1: Formulate the Research Question

The research question is the first and the most important step of medical research. If the research question is good, the research may or may not be good but if the research question is poor, the research definitely becomes poor. The most important aspect to be considered while framing a good research question is the "FINER" approach (Table 39.2).

One should be careful in avoiding waste of resources and intellectual energy while framing a research question. This can be done by (i) doing a pilot or proof of concept study, (ii) consulting a biostatistician beforehand to choose a less costly design and common outcomes, and (iii) calculating the feasibility of enrolling the intended number of subjects from the population of interest.

Once framed, the research question should be in the PICO (T) format (Table 39.3).

Table 39.4 Examples of flawed research questions

Question	Reason of flaw
What is the childhood BSI rate in my ICU?	Too narrow
What are the effects of ICU stay on quality of life in India?	Unfocused and too broad
How much time do pneumonia patients sleep daily?	Too objective
How many ICUs have an antibiotic protocol for meningitis?	Too simple

Table 39.5 Choice of study design according to the study objective

Study objective	Choice of design
Prevalence	Cross-sectional
Incidence	Cohort
Cause (in order of reliability)	Cohort, case-control, cross-sectional
Prognosis	Cohort
Treatment effect	Controlled trial

If the research question has never been studied and is interesting, it is worthwhile pursuing. If the scientific question has been answered before, the question can be modified to get an answer about some other behavior or variable.

Some examples of flawed research questions are shown in Table 39.4.

Step 2: Conceptualize the Study Design

The next important step is to choose the proper study design. This depends on the research question and the study objective. The choice of the design as per the study objective is shown in Table 39.5.

In this connection, it is important to recognize the differences in the study designs. There are two broad categories: observational and experimental. In observational, there can be case-control, cohort, and cross-sectional studies, while in experimental it is usually either randomized or nonrandomized clinical trials.

Table 39.6 shows some characteristics of the different observational and experimental studies.

While the biggest advantage of observational studies is the better generalizability due to high external validity their major drawback is the effect of bias due to low internal validity. This is the opposite of the randomized control trials. The randomized controlled trial (RCT) is the gold standard for determining the efficacy and adverse effects of any intervention.

Table 39.6 Different types of observational and experimental studies

Study design	Randomized control trial	Cross-sectional	Cohort	Case-control
Study population	Highly selected population, highly controlled environment	Diverse population observed in a range of settings	Diverse population observed in a range of settings	Diverse population observed in a range of settings
Directionality	Exposure is assigned before the outcome is ascertained	Exposure and outcome ascertained simultaneously	Exposure is ascertained before the outcome is ascertained	Outcome is ascertained before exposure is ascertained
Primary use	Demonstrating the efficacy of an intervention	Screening hypotheses, prevalence studies	Assessing the association between multiple exposures and outcomes over time	Assessing the association between exposures and rare outcomes
Analysis	Straight-forward	Sophisticated multivariate techniques may be required to account for confounding	Sophisticated multivariate techniques may be required to account for confounding	Sophisticated multivariate techniques may be required to account for confounding
Internal validity	High	Low	Low	Low
External validity	Low–moderate	High	High	High

Step 3: Construct an Instrument for Data Collection

The next step is to construct an instrument for data collection, which is called a case record form (CRF). One can choose either a paper or electronic document to record all the information required in a standard format. Both the study protocol and CRF must be designed in parallel to establish consistency between them.

The components of a standard CRF are shown in Table 39.7.

Figure 39.1 shows the differences between a poorly designed and well-designed CRF.

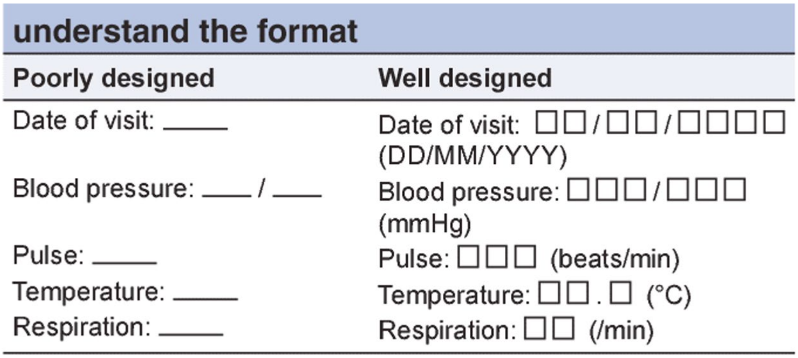
The general principles that should be followed while designing CRF are the following:

(a) When capturing dates, include a note of what format the date should be recorded in, e.g.,

Date of birth ☐☐ / ☐☐ ☐ / ☐☐☐☐ (DD/MM/YYYY)
(e.g. 01/JAN/2013)

Table 39.7 Components of an ideal CRF

Study title and number
Investigator’s name
Study subject/patient ID (number and initials)
Inclusion/exclusion criteria
Demographic data
Detailed description of dosage regimens of the investigational drug
Concomitant treatment
Adverse events (side effects and intercurrent diseases)
Conclusion on subject’s health
Investigator’s signature and date



understand the format

Poorly designed	Well designed
Date of visit: _____	Date of visit: ☐☐/☐☐/☐☐☐☐ (DD/MM/YYYY)
Blood pressure: ____/____	Blood pressure: ☐☐☐/☐☐☐ (mmHg)
Pulse: _____	Pulse: ☐☐☐ (beats/min)
Temperature: _____	Temperature: ☐☐.☐ (°C)
Respiration: _____	Respiration: ☐☐ (/min)

Fig. 39.1 Poorly designed versus well-designed CRF

(b) Coding wherever possible

(c) Use subscripts to note the variable codes (e.g., 1. Yes, 2. No) and be consistent with coding across all forms, e.g.,

DEMOGRAPHY	
Date of birth (DD/MM/YYYY)	☐☐ ☐☐ ☐☐☐☐
Gender	Male ☐ 1 Female ☐ 2
Height (cm)	☐☐☐ ☐
Weight (kg)	☐☐☐ ☐☐
Smoker	Yes ☐ 1 No ☐ 2
Family history	Yes ☐ 1 No ☐ 2

(d) Include units where applicable (e.g., mm Hg, ml/L, etc.)

(e) Collect raw data rather than calculated data; e.g., record the month and year of birth along with the visit date, rather than simply documenting the patient’s age in years

(f) Do not collect the same data twice, e.g., month/year of birth and age at the visit

Table 39.8 Sampling methods

Probability sampling	Nonprobability sampling
Simple random Stratified random Systematic Clustered random	Convenience Judgmental Snow-ball

(g) Remember to note whether the person completing the page should "Tick all that apply" or "Select one."
(h) Limit the use of free text to as little as possible
(i) Data collection should follow the flow of the study, and a CRF should only reflect data collected at one time point
(j) The finished product should be easy on the eye and logical in its execution

Step 4: Select a Sample

Sample means a group of people who share a common character or a condition. If we want to conduct a study on patients with sepsis, it will be difficult to include the whole population of sepsis all over the world. Therefore, the practical approach in clinical research is to include a part of this population, called "sample population," which is representative of the "target population," as much as possible with the least possible error and without substitution or incompleteness.

The process of selecting a sample population from the target population is called the "sampling method."

Table 39.8 shows the different sampling methods. It is advisable to get help from the Biostatistician or Senior Researcher while selecting the sampling method.

Step 5: Write a Research Proposal

It is mandatory for any research project to obtain the approval of IRB/IEC before its commencement. This is achieved upon expression of satisfaction by the IRB/IEC on certain basic points:

(a) The research project is worth undertaking for scientific gains.
(b) Investigator(s) have the necessary competence and work experience.
(c) No ethical violations and infringements of participants' rights.
(d) Requirements and limitations are adequately explained.
(e) All these are clearly documented in the research protocol (Table 39.9).

The protocol should be strictly adhered to during the entire period of study. Extra time spent on writing a good protocol will help at a later stage for analysis. If it is poorly prepared and not adhered to, it is unlikely to yield the information that is expected from research.

Table 39.9 Basic components of a research protocol

Title of the study
Administrative details
Project summary
Introduction to the research topic, background (literature review)
Preliminary studies
Study objectives and/or questions, statement of the problem.
Methodology: Study design, study population and methods of recruitment, variables list, sample size, methods of data collection, data collection tools, and plan of analysis (analysis of data)
Project management: Work plan (timeline—Proposed schedule)
Strengths and limitations of the study
Issues for ethical review and approvals

Table 39.10 Proper data collection methods and testing the validity of the instrument

Selecting a proper method of data collection	Establishing the validity of the data collection instrument
Primary sources: These are sources where information is collected directly from respondents for the specific purpose of the study being conducted. These include interviewing, observation, and use of questionnaires. *Secondary sources*: All other sources, where the information required is already available, viz., government publications, reports, and previous research, are called secondary sources	*Quantitative research* External consistency procedures: Test/retest and parallel forms of the same test Internal consistency procedures: Split-half technique *Qualitative research* Measured by two indicators: "Dependability" (paralleling reliability) and "confirmability" (paralleling objectivity)

Step 6: Collection of Data

This is an important step for the reason that wrong means of data collection can give rise to "GIGO" (garbage in garbage out) effect. This can be ensured by (i) selecting a proper method of data collection and (ii) establishing the validity and reliability of the data collection instrument (Table 39.10).

Step 7: Process and Display of Data

Since the data collected is "raw" data, its processing includes all operations undertaken from when a set of data is collected until it is ready to be analyzed either manually or by a computer.

This involves

(a) Data processing" starts with data editing (also known as basic "cleaning"), followed by coding of data, pre-testing it, coding per se, and verifying the coded data.

In the frame of analysis, the type of analysis to be undertaken (e.g., frequency distribution, cross-tabulation, content analysis) and applied statistical procedures should be specified.

Computers primarily help by saving labor associated with analyzing data manually.

Statistics are desirable though not essential for the study. Their extent of application depends upon the purpose of the study. Statistics primarily helps to generate a sense of data, "read" data, and explore and ascertain the magnitude of existing relationships or interdependence between variables, if any.

(b) Data presentation: In quantitative studies, the text is often combined with other forms of data presentation such as tables, graphs, and statistical measures. These make communication better, clearer, more effective, and easier to understand.

Tables have the advantage of containing a great deal of information in a small space. It has five parts: title, subtitles, column headings, body, and supplementary notes or footnotes. Depending upon the number of variables about which information in a table is stored, there are three types of tables: univariate (frequency), bivariate (cross-tabulation), and polyvariate. For its interpretation, simple arithmetic procedures such as percentages, cumulative frequencies, or ratios can be used. Other simple descriptive statistical procedures such as mean, median, or mode, chi-square test, t-test, and coefficient of correlation can also be used. In certain cases, advanced statistics can also be applied.

Graphs make it easy for readers to absorb information at a glance. While there are many types of graphs, the common ones are histogram, bar diagram, stacked bar chart, 100% bar chart, frequency polygon, stem-and-leaf display, pie chart, line or trend diagram, area chart, and scattergram.

The method of data presentation to be used is entirely based on the discretion of the researcher to suit his/her knowledge and comfort, which enhances the understanding of the research.

Step 8: Write a Research Report

It is a crucial step in the research process. A badly written report can spoil all the hard work that has been put into the research study.

There are certain obligations in terms of accuracy and objectivity. Before beginning to write the research report, it is necessary to develop a general outline. All sections should be written around the main themes of the study.

Abstract

Length can vary from one paragraph to several, but they follow the IMRAD format and typically spend 25% of their space on Introduction, 25% of their space on Methods, 35% of their space on Results, and 15% of their space on Conclusion. Abstracts do not discuss the study. They should not be too long.

Introduction

It is not a historical perspective or a review. It should not be vague and general. Don't put discussion material here. Stay sharp and focused.

Methods

What did we do? It describes the methodology to make the reader visualize how it was executed. It is written in past tense with a passive voice with headings and subheadings. It describes statistical tests for comparison of the data captured and the statistical software. Those working in this field would read it with interest; for others, it is the least-read section of an IMRAD report.

Results

What are the findings? What did we find? It is like presenting the findings and outcomes of the research. It contains tables and figures. It may contain things like forest plots, Kaplan–Meyer graphs, and ROC curves. All tables and figures are labeled and numbered separately. Captions go above tables and beneath figures.

Discussion

What does the study mean? What is the message/inference of the study? It may summarize the main findings/significant findings of the study, allowing the readers to skip reading the entire report. It is like the "headlines" in a news bulletin. If interested listen to the full broadcast. It connects these findings to other research. It discusses the strengths and flaws of the present study. It may include a concluding remark. It often mentions the limitations of the present study and suggests the need for future research. It may state the implications of their findings for future policy or practice.

Conclusion

An example of the conclusion of a research report could be as follows: The quality of care provided in ICUs worldwide has improved enormously over the past decade. Nevertheless, many disorders like ARDS (adult respiratory distress syndrome), sepsis, and hospital-acquired infections (HAIs) remain foci of interest and are difficult to manage and associated with high mortality rates. Consequently, further research studies on several fields are urgently needed.

Suggested Reading

Murad MH, Montori VM. How to read a systematic review and meta-analysis and apply the results to patient care: users' guides to the medical literature. JAMA. 2014;312(2):171–9. *Clinical decisions should be based on the totality of the best evidence and not the results of individual studies. When clinicians apply the results of a systematic review or meta-analysis to patient care, they should start by evaluating the credibility of the methods of the systematic review, i.e., the extent to which these methods have likely protected against misleading results.*

Sun X, Ioannidis JP. How to use a subgroup analysis: users' guide to the medical literature. JAMA. 2014;311(4):405–11. *This article provides five criteria to use when assessing the validity of subgroup analyses: (1) Can chance explain the apparent subgroup effect? (2) Is the effect consistent across studies? (3) Was the subgroup hypothesis one of a small number of hypotheses developed a priori with direction specified? (4) Is there strong preexisting biological support? (5) Is the evidence supporting the effect based on within- or between-study comparisons?*

O'Sullivan D, Wilk S. Using PICO to align medical evidence with MDs decision making models. Stud Health Technol Inform. 2013;192:1057. *PICO (evidence-based search strategy focusing on Patient/Population, Intervention, Comparison, and Outcome)-based framework for indexing and retrieving medical evidence. Students reported that the PICO-based framework for organizing evidence provided an intuitive way of accessing and evaluating evidence and would be useful for their clinical tasks.*

Speckman RA, Friedly JL. Asking structured, answerable clinical questions Using the population, intervention/comparator, outcome (PICO) framework. PM R. 2019;11(5):548–53. *An analysis of the PICO format for clinical research*

Artificial Intelligence in Critical Care

40

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Introduction

Over the past two decades, the severity of ICU patients and the intensity of therapeutic interventions have increased significantly. In complex diseases such as ARDS and sepsis exhibiting significant heterogeneity, efforts are being made to identify specific phenotypes to enable precision therapies. Additionally, the widespread availability of health-related information on the internet has heightened the cognitive demands on ICU physicians.

The rapid digitalization of healthcare records has enhanced transparency and emphasized data accuracy. Automated monitoring, charting, and trending systems now allow for early detection of clinical events. Advanced technologies provide partially or fully automated solutions for tasks such as hypoxia management, weaning, asynchrony detection, and ECG interpretation. Modern ICUs are rich in data, generating vast amounts of information that surpass the processing capabilities of traditional systems.

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Big Data in ICU

Big data refers to datasets of immense size, complexity, and dynamic nature, often measured in petabytes (10^{15} bytes). Big data analytics (BDA) employs diverse algorithms, including techniques like latent class analysis and causal mediation analysis, which have been utilized in ARDS research.

- The availability of big data provides fertile ground for developing precise predictive models, advanced decision-support tools, and personalized patient care.
- Open-access databases, such as the MIMIC (Multiparameter Intelligent Monitoring in ICU) database, which contains data from 40,000 ICU stays, allow data scientists to develop and validate analytical algorithms.
- Other notable databases include the ANZICS database (900,000 ICU stays), the Cerner APACHE outcomes database (150,000 ICU stays), and the Philips eICU database, which contains information on over 1.5 million ICU stays.
- Despite these advancements, challenges remain in ensuring the availability of large-scale big data for research due to data privacy concerns and regulatory constraints.

This chapter will give you a brief overview of the application of AI in health care and ICU.

Step 1: Understanding the Definitions of AI

Artificial Intelligence (AI)

Artificial Intelligence (AI) was first described by John McCarthy in 1956 as the science and engineering of creating intelligent machines. AI refers to the use of computers and technology to simulate human cognitive functions such as reasoning, decision-making, generalization, and learning from past experiences. It aims to replicate intelligent behavior and critical thinking comparable to the human brain.

Subsets of AI

1. *Machine Learning (ML)*:

   ML is a subset of AI and computer science that focuses on enabling computers to learn and improve from data and algorithms without explicit programming for every task.
   - *Supervised Learning*: The model is trained using labeled data with defined outcome targets.
   - *Unsupervised Learning*: The algorithm identifies patterns or groupings in data without predefined outcomes.
   - ML is widely applied in various industries for tasks such as fraud detection, marketing, strategic decision-making, and analyzing large, complex datasets.

2. *Deep Learning (DL)*:

   DL is an advanced form of ML that uses Artificial Neural Networks (ANNs) to analyze data in hierarchical layers of increasing complexity.

   - *Artificial Neural Networks (ANNs)*: Composed of multiple layers—input, hidden, and output—ANNs mimic the structure of the human brain. Nodes (neurons) in these layers are connected and activated if their output surpasses a certain threshold, passing data to subsequent layers.
   - *Deep Neural Networks*: Neural networks with more than three layers are referred to as "deep" networks. DL is particularly effective for tasks like image recognition, face detection, and interpreting radiology images.

3. *Natural Language Processing (NLP)*:

   NLP focuses on the interaction between computers and human language. It converts unstructured text, such as medical documents, into structured and analyzable data. NLP tools enable AI systems to understand, interpret, and generate human language effectively.

Applications of AI

AI has been integrated into daily life through tools like virtual assistants (e.g., Apple's Siri, Google Assistant, and Amazon's Alexa), which help perform defined tasks. In medicine, AI applications can be classified into:

- *Virtual AI*: Includes electronic health record systems and neural network-based treatment guidance.
- *Physical AI*: Includes robots for surgery, intelligent prosthetics for disabled individuals, and assistive devices for elderly care.

By understanding these definitions, we gain insight into AI's capabilities, its subsets, and its transformative potential across various domains.

Step 2: Understand the Types of AI and Their Utilities

Artificial narrow AI (ANI) or weak AI: Designed to perform certain tasks, and lacks general cognitive abilities. Examples include virtual assistants like Apple Siri and Amazon Alexa, and recommendation engines on streaming platforms.

Artificial general intelligence (AGI) or strong AI: It is capable of learning, understanding, and applying knowledge across various domains.

Artificial superintelligence (ASI): This theoretical model is capable of surpassing human intelligence in all aspects.

Generative AI: This type of AI creates new content, such as text, images, music, video, and virtual worlds. It uses ML to learn from data and then generates new data with similar characteristics.

Step 3: Introduction to AI in Healthcare and Intensive Care Units

- *Overview of AI Applications in Healthcare*:
  - Artificial Intelligence (AI) is transforming healthcare through its ability to analyze large amounts of data, recognize patterns, and improve decision-making.
  - Its applications range from clinical diagnosis and outbreak surveillance to medical imaging, education, and pharmaceutical advancements.
  - AI also assists in automating administrative processes like billing, insurance claims, and clinical trial management, thereby enhancing efficiency across the healthcare system.
- *Current State of AI in Intensive Care Units (ICUs)*:
  - In ICUs, AI is increasingly being used to manage critically ill patients.
  - Advanced AI-powered systems monitor patients in real time, identify early warning signs, and provide predictive analytics to support treatment decisions.
  - Applications include automating tasks like hypoxia management, ventilator weaning, and asynchrony detection.
  - AI helps ICU teams process vast amounts of data to improve outcomes for critically ill patients.

Applications of AI in Healthcare

1. *Clinical Diagnosis*:

   AI leverages deep learning and pattern recognition to analyze symptoms, medical records, and radiological images. It uses repetitive algorithms to identify specific patterns, aiding in accurate and timely diagnoses.
2. *Infectious Disease Surveillance*:
   - Early outbreak detection is facilitated through natural language processing (NLP) of news and social media data.
   - AI models like convolutional neural networks (CNNs) are used for pathogen identification, such as automating malaria microscopy or reading antibiograms.
   - Tools like mobile apps for measuring antibiotic sensitivity contribute to global antimicrobial resistance (AMR) surveillance.
3. *Radiology*:

   AI assists in triaging positive radiology films, detecting abnormalities, and quantifying changes using deep learning algorithms. Future advancements aim to integrate imaging data with patient history and nonimaging data to create customized interactive reports.
4. *Histopathology*:

   Machine learning supports histopathological tasks like cancer classification, tumor grading, cell identification, and treatment planning. Advanced models, including convolutional neural networks and graph neural networks, are integral to digital pathology.

5. *Medical Education*:

   AI, including large language models like ChatGPT, enhances medical education by simulating patient interactions and offering real-time coaching. These tools assist learners in asking relevant questions, interpreting findings, and preparing for clinical decision-making.
6. *Billing and Insurance Claims*:

   AI is increasingly used in billing systems to capture medical device usage and streamline insurance claims processing. It helps ensure accurate documentation and faster claim resolutions.
7. *Retrieval of Medical Information*:

   AI supports the integration of diverse patient information sources, enhancing diagnostic accuracy and facilitating the use of electronic medical records (EMRs).
8. *Clinical Trial Performance*:

   AI aids in trial design, patient recruitment, and monitoring outcomes and side effects, making clinical trials more efficient and effective.
9. *Pharmaceutical Industry*:

   AI accelerates drug development, ensures product quality, and assists in market analysis for proper pricing and positioning. It also helps optimize drug dosages for maximum efficacy.

Benefits of AI in Healthcare

- Enhances diagnostic accuracy.
- Improves efficiency and reduces healthcare costs.
- Supports personalized treatments and better patient outcomes.
- Streamlines administrative tasks, freeing up time for patient care.

Challenges of AI in Healthcare

- Ensuring data privacy and security.
- Integration with existing healthcare systems.
- Overcoming regulatory and ethical concerns.
- Balancing automation with human oversight to ensure fairness and transparency.

By integrating AI effectively, healthcare systems can leverage its full potential to revolutionize patient care and improve operational efficiency.

Step 4: Clinical Applications of AI in ICUs and Sepsis

1. *Predictive Modeling for Patient Outcomes and Risk Stratification in Sepsis*:
   - AI tools can analyze patient data to predict outcomes such as mortality and risk of complications. For example, the *AI Clinician Project* used data from MIMIC III to develop models that optimize fluid and vasopressor dosing in sepsis, resulting in lower mortality when clinical decisions aligned with AI recommendations.

- AI-based models also stratify risks for hospital-acquired infections like ventilator-associated pneumonia, enabling early preventive strategies.

2. *AI-Assisted Diagnosis and Decision Support Systems*:
    - AI enhances diagnostic precision in sepsis and other ICU conditions. For instance, the *Risk of Sepsis (RoS) Score* outperformed traditional tools like SOFA in identifying sepsis earlier, aiding timely interventions.
    - Machine learning models are also employed for diagnosing conditions like ARDS and stroke with high accuracy using imaging and clinical data.
3. *Personalized Medicine and Treatment Planning*:
    - AI enables personalized treatment strategies, such as optimizing fluid resuscitation in sepsis. Retrospective analyses show that AI-driven "caps" on fluid volumes reduce 30-day mortality.
    - AI tools can also refine ventilator management, as demonstrated by Google's DNN-based ventilator control solution, which predicts airway pressure changes in real time.
    - *Automated Monitoring and Alert Systems*:
    - Early warning systems like *CHARTWatch*® analyze patient data in real time to predict deterioration risks and reduce unanticipated ICU transfers and mortality. This tool analyzes more than 100 attributes ranging from history, and current health status from EMR.
    - This tool was examined in a large cohort of patients admitted to the medical ward and showed a significant 26% reduction in unanticipated mortality after the tool was implemented.
    - Wearable devices like *VitalPatch*® continuously monitor cardiac and respiratory parameters, enhancing early detection of arrhythmias and other critical conditions. It continuously gathers physiological data from the person being monitored and then transmits encrypted data via bi-directional communication to the relay device to facilitate continuous data transmission.
4. *Reduction in Critical Alarms*
    - Hospital units face a significant challenge with alarm overload, as 80–99% of alarms are false or clinically insignificant. This excessive noise can mask critical alerts, increasing the risk of missing life-threatening events.
    - An experimental AI model developed in Australia analyzed monitoring and vital signs data from 32 surgical patients who underwent anesthesia and demonstrated a remarkable 99.3% reduction in total alarms generated.
    - A comprehensive review further confirmed the efficacy of AI-driven intelligent alarm management systems. These tools effectively reduced false alarms, alarm durations, the frequency of nurse responses to critical alarms, and alarm fatigue among nursing staff.
5. *AI in Diagnostic Imaging*
    - In critical care settings, rapid and accurate interpretation of diagnostic imaging is vital to prevent delays that could compromise patient outcomes. AI-powered systems, particularly those using deep learning, have significantly enhanced the speed and precision of image analysis.

- By identifying subtle abnormalities, these systems support timely and accurate diagnoses of conditions like acute respiratory distress syndrome (ARDS), pulmonary embolism, and cerebral hemorrhages.
- Compared to traditional methods, AI facilitates faster and more reliable decision-making, improving patient care in high-stakes environments.

Step 5: Implementing AI in ICUs

1. *Data Collection and Integration*:

   AI relies on high-quality, interoperable data from sources such as EHRs, bedside monitors, and imaging systems. Integration of structured and unstructured data ensures comprehensive analysis.
2. *Algorithm Development and Validation*:

   Training AI models on diverse datasets and rigorous validation are critical for ensuring reliability. Models like the *UNETR* for ARDS prediction illustrate how advanced algorithms can identify clinical patterns that improve early diagnosis.
   - *ARDS Diagnosis Using AI*
     - Machine learning algorithms, trained on extensive datasets of chest X-rays, have shown the ability to detect subtle signs of acute respiratory distress syndrome (ARDS) that may be missed by human observers.
     - A convolutional neural network (CNN) trained on over 8000 chest X-rays achieved expert-level performance in identifying ARDS on radiographs.
     - In parallel, a robust computational framework based on the CheXnet algorithm—a deep learning model—was developed to identify pneumonia in chest X-rays. This model demonstrated an impressive accuracy of 92.47% in pneumonia detection.
     - The CheXnet-based neural network holds promise as an effective tool for automating pneumonia diagnosis in clinical settings, paving the way for enhanced efficiency and precision in medical imaging.
   - *Stroke Detection Using AI*
     - Deep learning-based AI systems enable rapid stroke detection, expediting the intervention process.
     - The Viz LVO algorithm analyzes head and neck CT angiograms (CTA) to identify large vessel occlusions (LVOs). Studies report high accuracy, with 93% sensitivity, 91% specificity, and a 99.7% negative predictive value for detecting occlusions in critical areas like the ICA terminus and middle cerebral arteries (M1 and M2).
     - Additionally, Viz LVO software has been shown to shorten the door-to-puncture time for patients needing endovascular treatment, improving overall outcomes.
   - *AI in ARDS: Risk Prediction, Diagnosis, and Ventilation Strategies*
     - AI is transforming the management of ARDS by improving diagnosis, risk prediction, and decision-making while reducing costs and enhancing outcomes.

    - Recent reviews show that AI-based models have been applied to diagnose ARDS, stratify risk, predict severity and mortality, and assist in clinical management, achieving high performance with area under the curve (AUC) values between 0.8 and 1.
    - An XGBoost gradient-boosted tree model was developed to predict ARDS up to 48 h before onset using clinical data and radiology reports. Similarly, in China, a deep learning-based UNet Transformer (UNETR) model using chest CT scans outperformed DenseNet in prediction accuracy. This model identified key predictors of ARDS, including lung lesion features, C-reactive protein, albumin, bilirubin, platelet count, and age.
    - As healthcare faces staff shortages, AI technologies will play a critical role in reducing the need for constant monitoring, minimizing human error, and ensuring timely interventions.
  - *Precision Dosing in Sepsis: Impact of Fluid Resuscitation*
    - A retrospective cohort study using data from the Medical Information Mart for Intensive Care III (MIMIC-III) explored the effects of fluid resuscitation on sepsis outcomes. By applying causal inference techniques, researchers estimated 30-day mortality rates under different fluid volume limits during the first 24 h of ICU care.
    - The analysis suggested that imposing caps on fluid administration between 6 and 10 liters could reduce 30-day mortality compared to current practices, with the greatest benefit observed at an 8-liter cap.
  - *HAIKU Project: AI for Hospital-Acquired Infections*
    - The HAIKU (Hospital-Acquired Infection Knowledge in Use) framework leverages AI to support physicians and infection control teams in detecting cases, stratifying risks, and identifying diagnostic factors.
    - Using advanced predictive techniques, HAIKU highlights the elevated risk of hospital-acquired infections, such as ventilator-associated pneumonia (VAP), in critical care patients.
    - The system analyzes patient data, including ventilator settings, test results, and historical infection rates, to identify individuals at higher risk for VAP. This enables early preventive interventions, improving patient outcomes and reducing infection rates.

3. *AI in Mortality Prediction and Workflow Optimization*
   Mortality Prediction Models
   - AI algorithms can predict ICU mortality using reinforcement learning-based models, outperforming traditional clinician-led approaches.
   - The AI Clinician Project at Imperial College London developed a model using 48 variables, including vital signs, lab results, fluid administration, and vasopressor use, sourced from the MIMIC-III database.
   - The best-performing model, selected from 500 iterations, was validated with the eRI dataset. Results showed the lowest mortality rates in patients where clinical decisions aligned with AI recommendations. This model offers personalized and interpretable treatment guidance for sepsis, improving patient outcomes.

4. *AI in Workflow and Resource Management*
    - In critical care units, AI enhances workflow and resource planning, reducing staff stress and optimizing care delivery. AI-powered tools predict staffing needs, resource use, and ICU bed occupancy, simplifying processes to reduce errors and improve efficiency.
    - *Example: Bed Management Algorithms*
        - AI tools forecast patient volumes by predicting emergency, elective, and inpatient admissions, as well as movements like ward transfers, readiness for discharge, and readmissions. These tools also aid in resource planning, estimating the demand for imaging, lab tests, and hospital length of stay, streamlining operations in high-pressure environments.
5. *Clinical Workflow Integration and User Adoption*:

    Seamlessly embedding AI tools into ICU workflows is essential. AI systems should offer user-friendly interfaces and actionable insights. Training staff and addressing usability barriers enhance adoption rates.
6. *Addressing Ethical and Regulatory Considerations*:

    Transparent AI processes that comply with regulations, such as the EU AI Act, safeguard data privacy and ensure ethical application. Policies must address challenges like bias, interpretability, and equitable access.

Step 6: Case Studies and Examples

1. *Real-World Examples of AI Implementation in ICUs*:
    - AI in Early Warning Systems: CHARTWatch reduced unanticipated mortality by 26% in hospitalized patients.
    - Mobile Antibiotic Resistance Monitoring: Smartphone apps for Kirby–Bauer disk analysis support global antimicrobial resistance (AMR) surveillance.
    - AI in Stroke Care: Viz LVO software identifies vascular occlusions on CT angiograms with high sensitivity and reduces intervention times.
2. *Success Stories and Lessons Learned*:

    Tools like AI-driven risk stratification for *Clostridium difficile* infections have been integrated into hospital workflows, improving prevention and patient outcomes.
3. *Future Directions and Ongoing Research*:

    Emerging trends include integrating AI with telemedicine and real-time actionable outputs. Future advancements will enhance personalized medicine, optimize resource use, and address workforce shortages.

Artificial intelligence is revolutionizing critical care, enhancing monitoring, diagnostics, treatment optimization, and resource allocation. While challenges like data integrity and ethical concerns remain, AI's potential to improve outcomes, efficiency, and precision medicine is substantial. Its seamless integration with clinical workflows will redefine ICU care, paving the way for smarter and more effective healthcare system.

Suggested Reading

Advances in Brownstein JS, Rader B, Astley CM, Tian H. Artificial intelligence for infectious-disease surveillance. N Engl J Med. 2023;27(388):1597–607. https://doi.org/10.1056/NEJMra2119215.

AI in healthcare: market dynamics, global trends, and the road ahead. Binariks radar. https://www.linkedin.com/pulse/ai-healthcare-market-dynamics-global-trends-road-ahead-binariks-htkaf/

Delahanty RJ, Alvarez J, Flynn LM, Sherwin RL, Jones SS. Development and evaluation of a machine learning model for early identification of sepsis in a multicenter cohort. JAMA Netw Open. 2019;2(12)

Fernandes CO, Miles S, De Lucena CJP, Dawn D. Artificial intelligence Technologies for Coping with alarm fatigue in hospital environments because of sensory overload: algorithm development and validation. J Med Internet Res. 2019;21(11):e15406. https://doi.org/10.2196/15406.

Hassan AE, Ringheanu VM, Preston L, Tekle WG. Artificial intelligence–parallel stroke workflow tool improves reperfusion rates and door-in to puncture interval. Stroke Vasc Interventional Neurol. 2022;2(5) https://doi.org/10.1161/SVIN.121.000224.

Le S, Pellegrini E, Green-Saxena A, Summers C, Hoffman J, Calvert J, et al. Supervised machine learning for the early prediction of acute respiratory distress syndrome (ARDS). J Crit Care. 2021;61:53–60.

Li B, Yue L, Nie H, Cao Z, Chai X, Peng B, et al. The effect of intelligent management interventions in intensive care units to reduce false alarms: an integrative review. Int J Nurs Sci. 2023;11(1):133–42. https://doi.org/10.1016/j.ijnss.2023.12.008.

Rashid M, Ramakrishnan M, Chandran VP, Nandish S, Nair S, Shanbhag V, et al. Artificial intelligence in acute respiratory distress syndrome: a systematic review. Artif Intell Med. 2022;131:102361. https://doi.org/10.1016/j.artmed.2022.102361.

Shaban-Nejad A, Riazanov A, Charland KM, Rose GW, Baker CJO, Tamblyn R, Forster AJ, Buckeridge DL. HAIKU: a semantic framework for surveillance of healthcare-associated infections. Procedia Comput Sci. 2012;10:1073–9. https://doi.org/10.1016/j.procs.2012.06.151.

Smit JM, Krijthe JH, Bommel JV. Causal inference for ICU collaborators. The future of artificial intelligence in intensive care: moving from predictive to actionable AI. Intensive Care Med. 2023;49(9):1114–6. https://doi.org/10.1007/s00134-023-07102-y.

Verma AA, Stukel TA, Colacci M, Bell S, Ailon J, Friedrich JO, et al. Clinical evaluation of a machine learning–based early warning system for patient deterioration. CMAJ. 2024;196(30):E1027–37. https://doi.org/10.1503/cmaj.240132.

Zhou Y, Mei S, Wang J, Xu Q, Zhang Z, Qin S. Development and validation of a deep learning-based framework for automated lung CT segmentation and acute respiratory distress syndrome prediction: a multicenter cohort study. eClinicalMedicine. 2024;75:102772.

Part VIII

ICU Procedures

Central Line Placement

41

Rajesh Chawla, Sudha Kansal, Roseleen Kaur Bali,
and Roopesh Banala

Case Vignette
A 55-year-old diabetic female patient was brought to the emergency department with history of fever with chills and rigors for the past 3 days. She also had altered sensorium for the past few hours. On arrival she was found to have tachycardia and hypotension.

Central venous access remains a cornerstone of resuscitation and is a commonly performed procedure in any ICU. The percentage of admitted patients with at least one intravascular catheter is approximately 90%, of which almost 18% are central venous catheters*. It is recommended to be performed real time under ultrasound guidance and it has improved success rates, reduced complication rates, decreased the time required to perform the procedure, and resulted in overall cost savings.

Step 1: Assess the Need for Central Line Placement

Insert a central line only for patients in whom it is indicated (as mentioned below) after ruling out contraindications (as mentioned in Step 2):

- For appropriate fluid management where peripheral access is difficult to get
  - Sepsis and septic shock
  - Low urine output

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  - Intraoperative
  - For patients in shock
- Concentrated vasoactive agent administration (e.g., norepinephrine >0.2 mcg/kg/min)
- Interventions like thrombolysis, venous stenting, and
- Difficult peripheral vascular access
- Multiple drug administration
- Concentrated electrolytes (e.g., potassium)
- Total parenteral nutrition
- Chemotherapy
- Agents irritating to peripheral veins (e.g., Amiodarone, Phenytoin, mannitol, concentrated potassium)
- Prolonged antibiotic therapy (e.g., endocarditis)
- Temporary hemodialysis
- ECMO
- During cardiopulmonary resuscitation
- Large-bore venous access for rapid administration of fluids
- For hemodynamic monitoring (ScVo2, CVP)
- Temporary transvenous pacing (pacemaker and defibrillator)
- Peripherally incompatible infusions

Step 2: Check for Any Contraindications

There are no absolute contraindications to central line placement. Relative contraindications are as follows:

- Local site infections or burns
- Anatomic abnormalities
- Coagulopathy/thrombocytopenia: Platelet count/P.Time/INR/APTT: safe levels in which central cannulation can be performed are unclear
- Thrombocytopenia poses a greater risk than clotting abnormalities
- No preprocedural correction is needed for platelet count >20,000 and INR <3.
- Use ultrasound guidance and an experienced operator

Coagulopathy, corrections needed if platelets <20,000 and INR >3 (ultrasound guidance will help in minimizing the risk of bleed and trauma).

The 2017 systematic review of central line placement in patients with coagulopathy or thrombocytopenia documented a wide range of bleeding incidences with major bleeding occurring in <1%*.

Step 3: Choose the Appropriate Site

The anatomic site chosen for central catheter placement influences the risk for any type of complications, including catheter-associated infection:

- Coagulopathy: Prefer—femoral > internal jugular > subclavian
- To decrease the risk of infection: Prefer—subclavian > internal jugular > femoral
- Right internal jugular vein cannulation is generally preferred over the left due to the larger diameter of the right-sided vein, its more direct path to the superior vena cava, the lower dome of the right pleura, absence of the thoracic duct, and the relative ease of access for a right-handed operator. Right-sided access is also associated with a low rate of catheter malposition.
- Right-handed operators often prefer right-sided subclavian access procedures. Right subclavian anatomy carries the theoretical advantage of lower risk of complications due to the lower pleural apex and absence of the thoracic duct. However, right-sided subclavian access is associated with higher rates of catheter malposition and vessel trauma compared with left-sided access. A left-sided access may be preferred when immediate cardiac access is needed (e.g., temporary transvenous pacer placement, pulmonary artery catheter) since the guide wire and catheter are more easily directed into the superior vena cava and right heart.
- Femoral lines are preferred if severe coagulopathy present, either left or right depending upon the operator.

Step 4: Choose the Appropriate Catheter

- Single-lumen or multi-lumen catheters*:* The more is the number of lumens, the smaller is their diameter.
- If rapid fluid infusion is required—as in trauma—single or double-lumen catheters are preferred.
- If the number of infusions is substantial, three- or four-lumen catheters are preferred.
- The infection risk is directly proportional to the number of lumens, so the more the number of lumens, the more the risk of infection associated with it.
- Antimicrobial-impregnated catheters*:* Can use a chlorhexidine/silver sulfadiazine or minocycline/rifampin-impregnated central venous catheter (CVC) in patients:
- When the catheter is expected to remain in place for more than 5 days or infection is more than 1.6 per 1000 catheter.

- The literature suggests that if the aseptic bundle along with a combination of antimicrobial CVCs, the rate of CLABSI could be lowered to a level below 0.5 case/1000 catheter days, to as low as 0.25 case/1000 catheter days*.
- The catheter infection rates are high in the ICU even after successful implementation of a comprehensive strategy to reduce rates of infection.
- Tunneled catheters*:* Tunneling is ineffective in decreasing infection rate in short-term CVCs.

Step 5: Know the Relevant Anatomy

- *The subclavian vein*: It crosses under the clavicle just medial to the midclavicular point. It lies underneath the clavicle at the insertion of the lateral head of the sternocleidomastoid on the clavicle. It is separated from the subclavian artery by the anterior scalene muscle, which lies deep to the vein. The vein lies in proximity to the dome of the pleura.
- *The internal jugular vein*: It is located in the neck at the apex of the jugular triangle formed by the two heads of the sternocleidomastoid muscle and the clavicle. At the apex, the carotid artery is medial and posterior to the vein.
- *The femoral vein*: It lies 1–1.5 cm medial to the femoral artery at the inguinal ligament. If the inguinal ligament cannot be identified as in obese patients, then the femoral artery lies approximately at the center of the pubic tubercle and the anterior superior iliac spine.

Step 6: Take Informed Consent

- Communicate with the patient or their surrogate.
- Explain the detailed procedure, the benefit, the risk, and the alternative in the language they understand.
- Reply to all the queries and concerns.
- Document the consent and get it signed.
- Have peripheral venous access before attempting central cannulation except probably during cardiopulmonary resuscitation.

Step 7: Keep all Equipment Ready for Cannulation and Pressure Transducing System

- Turn up the volume on the monitor so that it can be heard
- ECG, pulse oximetry, and BP monitoring instruments
- Material for sterile preparation—cap, mask, sterile gown, gloves and drapes (full body length).
- 2% chlorhexidine with alcohol
- Shoulder roll

- A 25-gauge needle and a syringe with 2% lignocaine
- Sterile saline flush
- A sterile cannulation set with CVCs, a guide wire, and a locator needle with the syringe
- A needle holder with suture material
- Sterile dressing
- The pressure transducing system.

Step 8: Set Up the Pressure Transducing System

This consists of a pressure transducing assembly with a flushing system.

Step 9: Obtain a Procedure-Directed History and Do a Physical Examination

- Location and number of previous CVCs
- Location of any known venous thrombi
- History of clavicle fracture
- History of IVC filter placement or pacemaker insertion
- History of any bleeding disorder or current use of anticoagulants
- History of allergy to chlorhexidine, povidone-iodine, or lidocaine
- History of pneumo/hemothorax. Cannulate the diseased site as it will have a chest tube.

Step 10: Central Line Placement

- Wear the cap and the mask.
- Wash hands with alcohol-based hand rub for 3–5 min and a minimum of three applications.
- Put on a sterile gown and gloves.
- Always do a procedural time-out to verify the procedure, site, and technique with team members.
- Always use sterile technique to prepare the skin and drape the patient.
- Clean the skin of the patient with more than 0.5–2% chlorhexidine in alcohol preparation. If this is not available povidone-iodine solution can be used.
- Give a frictional scrub circularly to at least 10 cm area from the insertion site.
- Do not shave if the hair is present, hair clipping is preferred.
- Place large sterile drapes over the insertion site. Do not occlude the air supply or field of vision when draping neck areas of conscious patients.
- 1–2% lidocaine for local infiltration before cannulation.
- Use Seldinger technique for cannulation
  - The desired vessel is punctured with a sharp, hollow needle called a trocar.

- A round-tipped (J-tipped), long guide wire is then advanced through the lumen of the trocar into the vessel.
- The trocar is withdrawn, leaving the guide wire in the vessel.
- The tract is dilated with a dilator introduced in a rotating motion.
- A hollow catheter can now be passed over the guide wire into the vessel.
- The guide wire is then withdrawn and the catheter remains in situ.
- Never lose control of the guide wire.
- Left subclavian vein for cardiac access, PA catheter, defibrillator.
- Avoid subclavian vein cannulation for dialysis due to the risk of thrombosis.
- Subclavian vein cannulation (Fig. 41.1)
  - Position should be Trendelenburg with the head turned toward the opposite side and a shoulder roll placed along the spine.
  - Stand on the side of the patient, where the procedure is planned.
  - Ensure maximum sterile barrier precautions.
  - Locate the landmarks, namely, the clavicle, sternal notch, sternocleidomastoid muscle, and its insertion on the clavicle, the lateral end of the clavicle (Table 41.1).

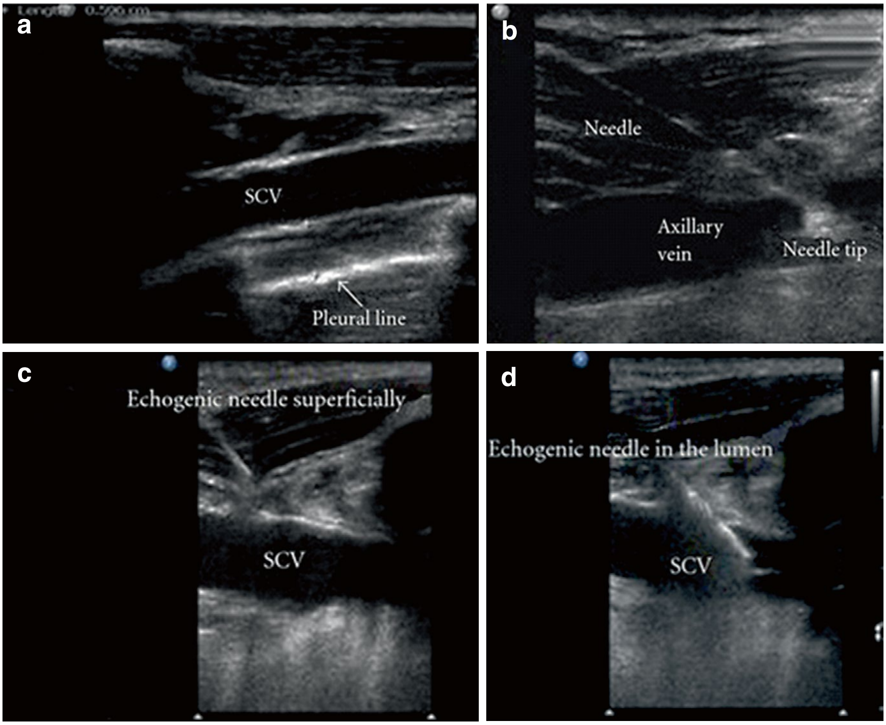

a
SCV
Pleural line
b
Needle
Axillary vein
Needle tip
c
Echogenic needle superficially
SCV
d
Echogenic needle in the lumen
SCV

Fig. 41.1 Location of Subclavian vein

Table 41.1 Approaches to subclavian vein cannulation

	Infraclavicular (common)	Supraclavicular
Insertion landmark	2 cm inferior to the midpoint of the clavicle and walk down the clavicle	Just above the clavicle, lateral to the clavicular head of the sternocleidomastoid
Angle with skin	0°	45°
Aim toward	Sternal notch	Contralateral nipple
Depth from skin	Just deep to the clavicle	1–2 cm, just under the clavicle

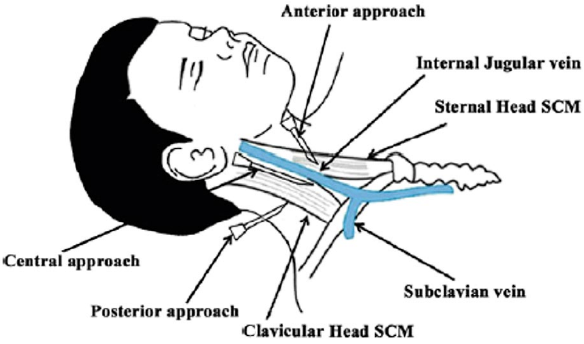
- Apply generous local anesthesia.
- Insert the needle and syringe (filled with 1–2 mL saline), constantly aspirating for venous blood (Fig. 41.1).
- If the rapid flush of blood does not appear during insertion of the needle, gradually withdraw the needle constantly aspirating. Blood may now appear.
- If the first attempt is unsuccessful, then withdraw the needle up to the skin and reposition the needle.
- Cannulate the vein using Seldinger technique as described above.
- Ensure backflow in all ports and flush all the ports.
- Ensure local hemostasis.
- Fix the catheter appropriately.
- Apply sterile dressing.
- *Internal jugular vein* cannulation (right IJV preferred due to risk of malposition)
  - Position should be Trendelenburg with the head turned toward the opposite side.
  - Stand at the head end of the patient.
  - Feel for the carotid and always keep it under your fingers.
  - Insert the needle at the following landmark and cannulate in a similar manner to subclavian vein (Table 41.2, Fig. 41.2).
- It is preferable to first locate the vein with a 25-gauge needle (finder needle) and then puncture with the larger needle.
- Cannulate using Seldinger technique.
- Obtain the chest X-ray after cannulation.
- *Femoral vein cannulation* (Fig. 41.3)
  - Position should be supine with the leg slightly abducted and externally rotated.
  - Stand on the side of the patient.
  - Insert the needle 45° angle to the skin at a point 1–1.5 cm medial to the femoral arterial pulsation and about 2–3 cm below the inguinal ligament.
  - Direct the needle cephalad toward umbilicus.
  - Cannulate using Seldinger technique.

Table 41.2 Approaches to the internal jugular vein (Fig. 41.2)

	Central	Anterior	Posterior
Insertion landmark	Apex of the triangle formed in the neck by the two heads of the sternocleidomastoid muscle and the clavicle[a]	Medial edge of the sternocleidomastoid muscle at level of thyroid cartilage	Lateral edge of sternocleidomastoid muscle, one-third of the way from the clavicle to the mastoid process
Angle with skin	45°	45°	30–45°, dive under the border of the sternocleidomastoid muscle
Aim toward	Ipsilateral nipple	Ipsilateral nipple	Sternal notch
Depth from skin	Within 3 cm	Within 3 cm	Within 5 cm

[a] If the vein is not encountered, then enter the skin slightly more medially and retry (Fig. 41.2)

Fig. 41.2 Approaches to the internal jugular vein


Anterior approach
Internal Jugular vein
Sternal Head SCM
Central approach
Subclavian vein
Posterior approach
Clavicular Head SCM

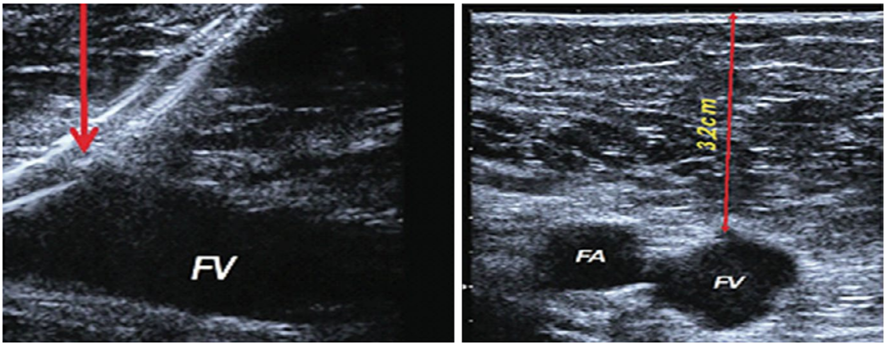

FV
3.2cm
FA
FV

Fig. 41.3 Short and long axis femoral vein

- *Ultrasound use for vascular access*
- This can be used in various ways as mentioned below.
  - *Precannulation ultrasound*, performed before insertion, is used to assess venous anatomy and patency. This examination helps in selecting the most suitable access site for the procedure.

  - *Intraprocedural ultrasound* is recommended for all patients undergoing central venous access, as it decreases complications and shortens cannulation time, especially in high-risk patients (e.g., those with coagulopathy). Essential steps include real-time needle guidance, guidewire position confirmation, and tip recognition to prevent catheter malposition.
  - *Post-cannulation ultrasound*, performed during or after the procedure, helps confirm the position of the guidewire and catheter tip and can detect procedure-related pneumothorax early.

Advantages

- Fewer complications
- Fewer attempts for successful cannulation
- Fewer failed procedure
- Shorter time for procedure (can be used in emergency situations)
- Can be used in patient with contraindication to blind technique; patient with coagulopathy
- Can be used in "difficult access" category; obesity, short neck, swollen neck, burns/postradiotherapy/postsurgical contracture, and so on.
- Decrease need of postprocedure radiological confirmation
- Complications such as arterial puncture were reduced from 16% to 5% in internal jugular and 5.8% to 0.8% in subclavian.
- *B mode ultrasound*
  - B mode ultrasound allows for detailed evaluation of vascular anatomy.
- *Transducer selection*
  - For central venous cannulation, high-frequency transducer (5–7 MHz) is ideal. Though in obese patients you may require low-frequency transducer.
- *Technique*
- USG guidance can be:
  - Precannulation vein assessment—Before cannulation, routine bedside ultrasound by the provider placing the access aims to evaluate the vein location, size, and patency and aids in selecting the most appropriate site of access. USG is used to localize the venipuncture site.
  - Real-time ultrasound guidance—recommend to use real-time ultrasound guidance during central venous cannulation at any site when it is available and practical to use.
- *View*
  - Transverse view: here cross-section view of vessel is obtained.
  - Longitudinal view: here longitudinal view of the vessel is obtained.
  - Oblique view: here the probe is slightly tilted 60° to obtain better orientation. Useful in collapsed vessels.
- *Method of orientation*

  The transducer has an identification mark on one side, which corresponds to mark displayed on one side of image, or alternatively finger can be rubbed on one side of transducer surface to produce an image and confirm orientation.
- *Procedure IJV (*Figs. 41.4 and 41.5*)*

Fig. 41.4 Central line cannulation under USG guidance

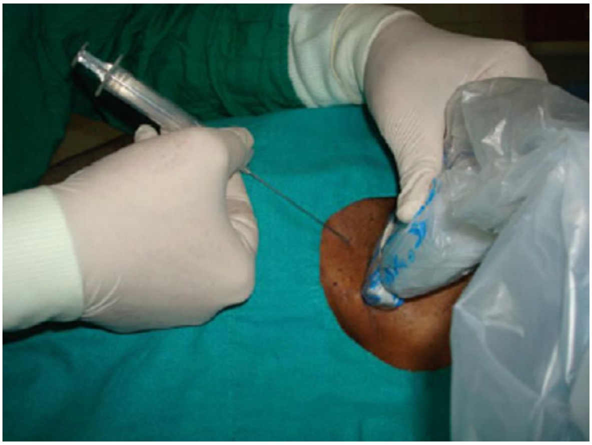
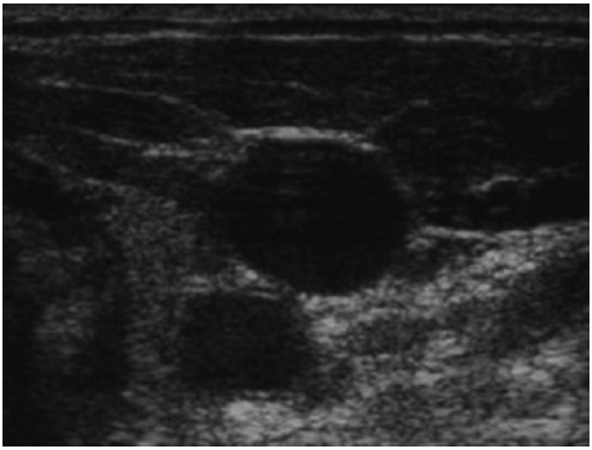


Fig. 41.5 Ultrasonographic transverse view of internal jugular vein (*above*) and common carotid artery (*below*)



- Position the patient in supine Trendelenburg position.
- Turn head to other side.
- Identify the landmark and select the site of puncture.
- Place the USG machine on ipsilateral side.
- Confirm the site puncture with ultrasound.
- Use transverse and longitudinal view to identify the structure around the vein.
- Can use Doppler to differentiate between vein and artery (depending on the flow velocity).
- Identify if there is any thrombus inside the vein
- The procedure should be performed under strict aseptic protocol (as described).
- Skin is prepared as described.
- The assistant holds the transducer and applies ultrasound gel over it.
- A sterile sheath (camera cover; used in laparoscopy) is placed on the sterile field.
- The operator takes the transducer from the assistant, ensuring that the transducer is covered in the sterile sheath. To maintain sterility, sterile sheath is also stretched

over the cord. Then apply band available with the sheath over the transducer to secure the sheath.

- Reconfirm the site of puncture. Can apply chlorhexidine over the transducer if image is not clear.
- Ensure that the vessel to be punctured is in the center of screen so that the vessel is lying just deep to the center of transducer.
- A dummy poke can be done by laying the needle on the skin surface and then pressure is applied near the tip of the needle, and visualize acoustic disturbance in the subcutaneous tissue due to this to ensure that it is positioned directly over the needle.
- Perform the skin puncture proximal to transducer, and while puncturing the subcutaneous tissue, ensure that the needle tip is seen advancing. If the tip is not seen, move the probe along the axis of the vein.
- Advance the needle further and visualize the needle tip entering the vessel lumen. Aspirate with the syringe to confirm the flash of blood.
- Reconfirm the needle position on the ultrasound.
- Now keep the probe aside in sterile environment.
- Proceed as before with placement of guide wire (Seldinger technique).
- Once the line is placed, reconfirm the position of line with the transducer by scanning distally.
- Examine with the probe for any pneumothorax.

Disadvantages

- Cost and maintenance of equipment
- Special USG training for operator
- Difficulty to maintain sterility during procedure

Step 11: Check the Post-Central-Line Chest X-Ray

The chest X-ray should be done after a subclavian and internal jugular cannulation. The following points should be noted in the X-ray:

- Catheter tip location
  - Catheter tips located within the heart or below the pericardial reflection of the superior vena cava increase the risk of cardiac perforation and fatal cardiac tamponade.
  - Ideally, the catheter tip should lie within the superior vena cava, parallel to the vessel walls, and be positioned below the inferior border of the clavicle and above the level of the third rib, the T4 to T5 interspace or the tracheal carina.
- Pneumothorax
- Pleural fluid/hemothorax
- Connecting with the transducer differentiate venous vs. arterial cannulation.
- Position can be confirmed by bedside USG, TEE, or newer techniques such as endocavitatory electrocardiography.

Step 12: Remove the Line

- As soon as it is not required
- Induration, redness, or frank pus discharge from insertion site
- Suspected or confirmed catheter-related infection
- Catheter occlusion/thrombosis
- Vascular erosion caused by the catheter

Step 13: Manage Complications

- *Mechanical complications* (Table 41.3)
- Never force the guide wire or the catheter; it may cause rupture of the vessel or injury to nearby structures.
- Do not over dilate—dilating the skin and subcutaneous tissue may be enough.
- During internal jugular vein and femoral vein puncture, always keep one hand over the artery to prevent arterial puncture.
- Never lose control of the guide wire, and hold it in one hand.

Table 41.3 Management of mechanical complication

Complication		Management
I. Vascular		
1.	Arterial puncture	Press the artery for at least 15 min or until bleeding stops
2.	Venous bleeding	Compress till bleeding stops
3.	Hematoma	
4.	Hemothorax	Correct coagulopathy, if any; may need drainage if massive
5.	Cardiac tamponade	
	Cardiac perforation	Surgical intervention
6.	Thoracic duct injury, chylothorax	Usually conservative
II. Pneumothorax		Always put an intercostal tube drainage if the patient is on positive-pressure ventilation
		If tension pneumothorax is present, release immediately with the needle thoracocentesis and follow with tube drainage
		Small pneumothorax in the spontaneously breathing patient can be kept under close observation
III. Air embolism		Always position the patient flat if the head is not down while inserting the line
		Never leave the lumen of the catheter uncapped
		If suspected, place the patient the right side up and the head down and aspirate blood mixed with air
IV. Nerve injuries		Conservative management
V. Tracheal/laryngeal injury		May need intubation
VI. Arrhythmia		Pull out the catheter till it is in the superior vena cava
VII. Malposition		May need repositioning

- When there is increased risk of bleeding, internal jugular vein route is preferable (with ultrasound guidance).
- *Infectious complications* (Table 41.4)

The following methods are required to prevent infectious complications:

- Use the line only when necessary and remove it as soon as it is not required.
- Use the subclavian vein and avoid femoral or internal jugular vein cannulation.
- Use a CVC with the minimum number of ports or lumens essential.
- Chlorhexidine skin antisepsis—A chlorhexidine solution should be applied by back-and-forth rubbing for at least 30 s. The solution should be allowed to air dry for at least 2 min and should not be wiped or blotted. Chlorhexidine appears preferable to a povidone-iodine solution.
- Use sterile gauze and sterile dressing to cover the catheter site.
- If the patient is diaphoretic or if the site is bleeding or oozing, use a gauze dressing until this is resolved, cap the lumen of port when not required.
- Replace dressings used on short-term CVC sites every 2 days for gauze dressings and every 7 days for transparent dressings.
- Use a chlorhexidine-impregnated sponge dressing if the infection rate is not decreasing despite adherence to basic prevention measures.
- Use a 2% chlorhexidine wash for patients' daily skin cleansing, not the insertion site.
- Evaluate the catheter insertion site daily for signs of infection.
- Use a suture less securement device.
- Use a chlorhexidine/silver sulfadiazine or minocycline/rifampin-impregnated CVC in patients whose catheter is expected to remain in place for more than 5 days or if the high infection rate is expected.
- Use povidone-iodine antiseptic ointment or bacitracin/polymyxin B ointment at the hemodialysis catheter exit site after catheter insertion and at the end of each dialysis session.
- Do not use guide wire exchanges to replace a catheter suspected of being source of infection.
- Lipid containing parenteral solution should be infused within 24 h.
- Clean access port with 70% alcohol and transfuse blood products over not more than 4–5 h.
- Heparin bonding in catheter used in oncology patients.

Table 41.4 Infectious complications

1. Insertion site infection	Remove the line and treat the infection
2. Catheter-related blood stream infection (CRBSI)	
3. Endocarditis	

Suggested Reading

Biffi R, Orsi F, Pozzi S, Pace U, et al. Best choice of central venous insertion site for the prevention of catheter-related complications in adult patients who need cancer therapy: a randomized trial. Ann Oncol. 2009;20(5):935–40. *Central venous insertion modality and sites had no impact on either early or late complication rate, but US-guided subclavian insertion showed the lowest proportion of failures*.

Hanna H, Benjamin R, Chatzinikolaou I, Alakech B, Richardson D, Mansfield P, Dvorak T, Munsell MF, Darouiche R, Kantarjian H, Raad I. Long-term silicone central venous catheters impregnated with minocycline and rifampin decrease rates of catheter-related bloodstream infection in cancer patients: a prospective randomized clinical trial. J Clin Oncol. 2004;22(15):3163–71. https://doi.org/10.1200/JCO.2004.04.124. Erratum in: J Clin Oncol. 2005 May 20;23(15):3652.

Hind D, Calvert N, McWilliams R, et al. Ultrasonic locating devices for central venous cannulation: meta-analysis. BMJ. 2003;327(7411):361. *A real-time two-dimensional ultrasound guidance for cannulating the internal jugular vein in adults was associated with a significantly lower failure rate both overall and on the first attempt.*

McGee DC, Gould MK. Preventing complications of central venous catheterization. N Engl J Med. 2003;348(12):1123–33. *NEJM current concepts series—a lucid description of the insertion maintenance and complications of central venous catheters.*

O'Grady NP, Alexander M, Burns LA, et al. Guidelines for the prevention of intravascular catheter-related infections. Am J Infect Control. 2011;39(4 Suppl 1):S1–34. *The latest version of the CDC guidelines for the prevention of intravascular catheter-related infections discusses in detail and provides recommendations on all aspects of catheter care and CRBSI reduction*.

Pérez-Granda MJ, Guembe M, Rincón C, Muñoz P, Bouza E. Effectiveness of a training program in compliance with recommendations for venous lines care. BMC Infect Dis. 2015;15:296. https://doi.org/10.1186/s12879-015-1046-1. Erratum in: BMC Infect Dis. 2016 June 27;16(1):313. https://doi.org/10.1186/s12879-016-1619-7. PMID: 26223265; PMCID: PMC4520149.

Ruesch S, Walder B, Tramèr MR. Complications of central venous catheters: internal jugular versus subclavian access—a systematic review. Crit Care Med. 2000;30(2):454–60. *This study shows significantly more arterial punctures with jugular catheters compared with subclavian. There are significantly less malpositions with the jugular access. They further show that the incidence of bloodstream infection is less with subclavian. Internal jugular vein cannulation using dynamic guidance of ultrasound in the transverse view.*

van de Weerdt EK, Biemond BJ, Baake B, Vermin B, Binnekade JM, van Lienden KP, Vlaar APJ. Central venous catheter placement in coagulopathic patients: risk factors and incidence of bleeding complications. Transfusion. 2017;57(10):2512–25. https://doi.org/10.1111/trf.14248. Epub 2017 Aug 30. PMID: 28856685.

Arterial Catheterization

42

Sheila Nainan Myatra, Mohd Saif Khan,
and Abhishek Singh Ranbahadur Singh Rajput

Case Vignette
A 65-year-old diabetic male patient was admitted to the ICU with right lobar pneumonia. He was started on appropriate antibiotic therapy. He was receiving oxygen by a mask at 8 L/min and maintaining a SpO_2 of 94%. His blood pressure was being monitored every 10 min using noninvasive blood pressure measurement. By evening his blood pressure started dropping and reached to 80/50 mmHg at 8 p.m., which was not responding to fluid boluses.

Intermittent noninvasive blood pressure monitoring methods such as oscillometry overestimates and underestimates the blood pressure in low- and high-flow states, respectively, thereby showing clinically important differences as compared with invasive arterial pressure monitoring. Invasive arterial pressure monitoring, using arterial catheterization, is one of the commonly performed bedside procedures in the ICU during shock, when noninvasive blood pressure monitoring, including continuous and intermittent methods, becomes unreliable.

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Step 1: Assess the Need for Intra-Arterial Pressure Monitoring Indications

- Hemodynamic instability
- Need for continuous blood pressure monitoring during vasoactive drug therapy
- Need for frequent arterial blood gas analysis (e.g., measuring paO_2, $paCO_2$, and pH, base deficit, arterial lactates, and electrolytes in the critically ill or during major surgery with anticipated blood loss or major fluid shifts)
- Assessment of fluid responsiveness using pulse pressure variation or stroke volume variation
- Fine tuning of target blood pressure in management of hypertensive emergencies requiring parenteral vasodilator therapy.

Step 2: Check for Any Contraindications

- Inadequate circulation to the extremity
- Uncontrolled severe coagulopathy
- Extremities with full thickness burn or trauma
- Skin infection over the insertion site
- Raynaud's phenomenon
- Multiple punctures or arterial cannulation in the past
- Thromboangiitis obliterans (Buerger's disease)
- Locations near arteriovenous fistulas

Step 3: Choose the Appropriate Site

- The radial artery at the wrist is the most preferred site as the hand has usually good collateral supply, and it is easy to access and maintain.
- Acceptable alternate sites commonly used in adult patients include the femoral, axillary, brachial, and dorsalis pedis arteries.
- All sites are at a risk of ischemic complications due to their small caliber (radial and dorsalis pedis), lack of good collateral supply (brachial and axillary), and presence of atherosclerotic vascular disease (femoral and dorsalis).
- Although infectious complications may be higher with the femoral artery, this may be the only palpable artery amenable to cannulation during severe hypotension. Only alternative to femoral artery for central blood pressure measurement is axillary artery. Ultrasound guidance has demonstrated utility in locating and cannulating the radial, dorsalis pedis, and femoral artery.
- Keeping in mind the above, always choose an artery you are familiar with cannulating.

- When the patient is on high-dose vasopressor therapy, the radial arterial site underestimates the intra-arterial blood pressure than femoral arterial site; therefore, it is advisable to use femoral arterial site in such scenario to optimally titrate the vasopressors.

Step 4: Check Perfusion of the Extremity

- Perform a *Modified Allen's test*:
  - The patient's hand should be elevated above his or her heart.
  - The patient should "clench the fist" for 30 s.
  - Pressure should be applied to both the radial and the ulnar artery until distal blood flow is occluded.
  - While maintaining the elevated hand position, the patient should then open the hand. The hand should appear pale and have limited capillary refills.
  - The ulnar arterial pressure should be released (while maintaining enough pressure to occlude the radial artery).
  - The hand should return to normal color within 5–7 s.
  - Delayed return suggests poor collateral circulation.
  - The test should then be performed on the radial artery circulation in the same manner.
- In the original *Allen's test*, the patient is asked to clench both fists tightly for 1 min, pressure is applied over both radial arteries simultaneously to occlude them. The patient then opens the fingers of both hands, the color of both is compared. The initial pallor should be replaced quickly by rubor. The test is then repeated by occluding both the ulnar arteries.
- In sedated or unconscious patient, to make the interpretation more objective, plethysmographic waveform analysis using pulse oximeter (Barbeau test) or doppler ultrasound examination may be used along with the *Modified Allen's test*. *Barbeau test* is performed by placing pulse oximeter probe over the thumb or index finger and then compressing the radial and ulnar artery simultaneously until the plethysmographic waveform disappears. This is followed by relieving pressure over the ulnar artery. In case of good collateral flow from ulnar artery, waveform appear immediately once the pressure over ulnar artery is relieved.
- The operator should document the impression of collateral circulation in the procedure note.
- Although the value of these tests has not been established, it may provide some qualitative assessment of collateral circulation. Routine application of Allen test or Barbeau test is not a useful triage strategy and an abnormal test should not preclude canulation. Due to the presence of dual supply and good collateral supply through intraosseous arteries to hand, radial artery occlusion (RAO) after radial artery cannulation is not clinically relevant. An occluded radial artery that fills via retrograde collaterals can be detected by the use of ultrasound or a reverse Allen or Barbeau test.

Step 5: Keep all Equipment Ready for Arterial Cannulation and Pressure Transduction

- Material for sterile preparation: Chlorhexidine 2% solution, gauze pieces, cap, gown, mask, gloves, sterile drapes.
- A wrist board or roller pad under the wrist, 25-gauge needles, and syringes with 1% lidocaine.
- An arterial catheter (three commonly available types):
  - Catheter with a needle (cannula over needle)
  - Catheter with needle and a guidewire separately (cannula over guidewire)
  - Catheter with needle and guidewire together (integral guidewire technique)

  Cannulate for arterial placement should be without an injection port and preferably have an eye to take a stitch.
- A needle holder with suture material.
- Sterile dressing (preferably transparent).
- An arterial connector.
- A pressure transducing system.

Step 6: Set Up the Pressure Transducing System

This consists of a pressure transducing assembly with a flushing system. The accuracy of the intra-arterial blood pressure measurement will depend on the proper setup and function of the pressure transducing system.

- *The pressure transducing assembly* consists of a coupling system, pressure transducer, amplifier, signal conditioner, analog to digital converter, and microprocessor that converts the signal received from the artery into a waveform on the bedside monitor.
- *The flushing system* is set up using a 500-mL normal saline bottle encased in a bag pressurized to 300 mmHg. At this pressure, the catheter will be flushed with 3 mL saline per hour and help keep the catheter patent. Using the flushing device helps flush the assembly as required. Before connecting flush, the pressure transducing system with saline using the flushing device removes all air bubbles and keep it ready to connect to the arterial catheter. Heparinized saline is no longer routinely used because of concerns about heparin-induced thrombocytopenia. In addition, continuous heparin flush solution has been shown to affect coagulation studies if the sample is drawn via the arterial line.

Step 7: Positioning and Preparation Prior to Radial Artery Cannulation

- Inform the patient about the procedure (if conscious) and take the informed consent.
- Position the wrist in dorsiflexion. This brings the radial artery in closer approximation to the skin and can be instrumental in the success of the procedure.
- This position can be maintained using a roll of gauze below the wrist or with a specially designed arm board and securing the arm with tape.
- Don a mask, cap, sterile gown, and gloves.
- The field can be sterilely prepared and draped using towels. In all invasive procedures, meticulous care should be taken to minimize the risk of infection.
- A small wheal of 1% lidocaine should be raised in the conscious patient to decrease the pain during cannulation and taking stitch.

Step 8: Radial Arterial Cannulation

Blind approach: The radial artery is palpated between the distal radius and the flexor carpi ulnaris tendon. The arterial catheter with needle is inserted at a 30–45° angle toward the artery.

Over-the-Needle Technique

Once there is blood return, the needle is advanced slightly further to ensure the catheter has entered the vessel. The needle angle is then lowered to 10–15°, and the catheter is guided over the needle and advanced into the vessel.

Over-the-Wire (Seldinger) Technique

- When blood return is noted, the catheter is advanced further, and the needle is then removed. The guidewire is then kept ready, and the catheter is withdrawn till there is pulsatile blood flow. The guidewire is inserted into the vessel, the catheter is advanced over it, and then the guidewire is removed.
- A commonly used variant of this technique is to initially insert only the introducer needle without catheter and then advance guidewire through the needle when in position, remove the needle and finally arterial catheter is advanced over the guidewire.

Integral Guidewire Technique (Over-the-Needle and Wire Technique)

- This is a special cannula-needle-guidewire assembly in which, when blood back flow is observed in long hub, the guidewire is advanced freely and then catheter is advanced over the guidewire and needle (Fig. 42.1).
- This is a quick and easy technique, associated with less blood loss as may occur with the other two techniques.

Real-Time Ultrasonography-Guided Arterial Line Cannulation

- This can be performed in centers where an ultrasonography (USG) machine and the expertise in USG-guided arterial line insertion is available. Success rate of radial arterial cannulation is higher with the use of USG-guided cannulation. This technique is especially suitable for critically ill patients with feeble pulse (hypotensive), obese, and edematous cannulation site.
- Ultrasound can also help to choose the appropriate size and length of the catheter. In a 2D view, the diameter of the arterial lumen is measured in mm. The

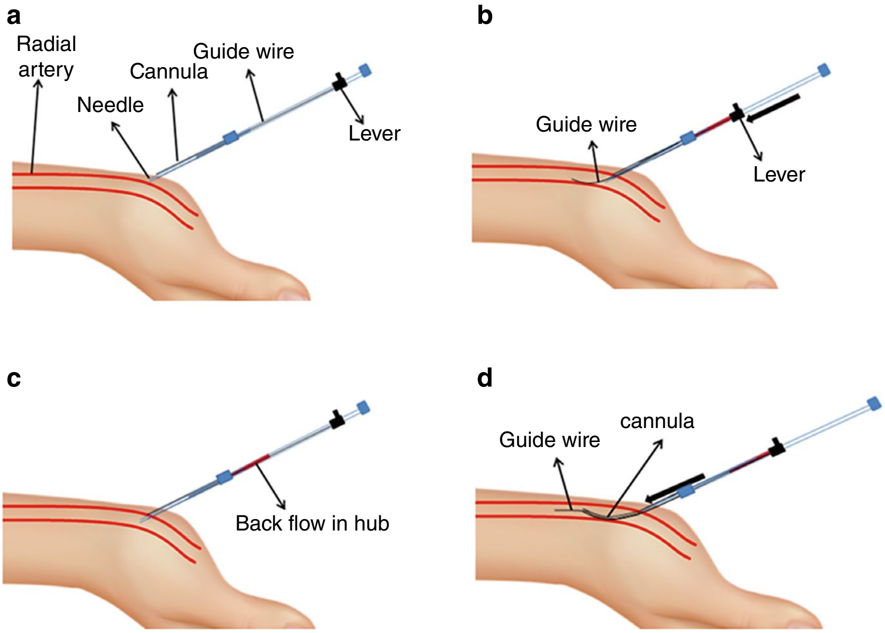

Fig. 42.1 Integral guidewire technique: (**a**) Needle is advanced at 45° to the skin, (**b**) radial artery puncture will be indicated by backflow in the tubing connected, (**c**) advance the lever to push guidewire freely into the arterial lumen, (**d**) cannula is advanced over the guidewire and needle and then the guidewire is removed

outer diameter of the selected arterial catheter should be less than 50% of the diameter of the arterial lumen. This helps ensure that there is sufficient blood flow around the catheter, reducing the risk of arterial occlusion and ischemia. A sterile probe cover or a sterile glove may be used to cover the ultrasound probe, as a barrier to prevent cross-contamination. Full aseptic precautions are taken during cannulation.

- Two approaches are commonly used to visualize the artery and its catheterization:
  - *In-plane approach.*

    In this approach, the radial artery is scanned in-plane (the long axis of probe is kept in line with long axis of artery so that it scans longitudinal section of artery). The advantage of this approach is real-time visualization of tip of needle entering inside the lumen. However, it requires expertise to hold and stabilize the probe during the procedure (Fig. 42.2).
  - *Out-of-plane approach.*

    This technique is easier to learn and quick. In this method the long axis of probe is perpendicular to long axis of artery in such a way that a transverse section of artery is visualized on the screen. The disadvantage is the loss of real-time entry if one is not careful about moving the probe in the direction of needle entry and may result in through and through puncture of arterial wall and posterior wall hemorrhage. The "target sign" is the end point in this technique when one can see bright spot (needle tip image) inside the lumen of artery.
- The success of either approach is heralded by free and pulsatile back flow of blood in the needle hub.

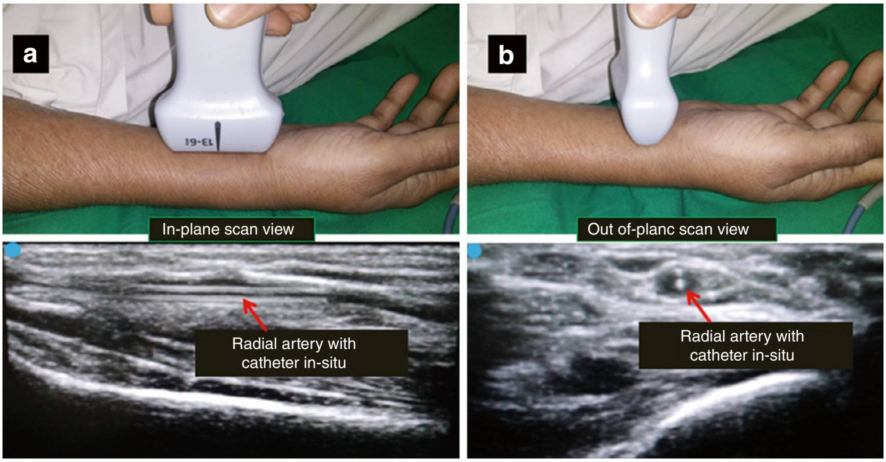
a
13-61
In-plane scan view
Radial artery with catheter in-situ
b
Out of-planc scan view
Radial artery with catheter in-situ

Fig. 42.2 Ultrasound views of radial artery. (**a**) In-plane scan view of radial artery is obtained when the long axis of probe is parallel to the long axis of the artery. (**b**) Out-of-plane scan view of radial artery is obtained when the long axis of the probe is kept perpendicular to the long axis of artery

Anticipated Difficulties During Cannulation

- In the over-the-needle technique, sometimes there is a blood return, but the artery cannot be cannulated. This may be because the needle has entered into the vessel lumen, but the catheter is still outside it. This can be overcome by advancing the needle further and then guiding the catheter over it. In another technique, advance the needle by 1–2 mm and remove the needle and look for pulsatile blood flow, then pass a guidewire into the vessel over which the catheter can be advanced easily.
- Sometimes the catheter may not easily pass through the skin. To overcome this, make a small nick on the skin with a needle or a blade at the insertion site.
- After multiple attempts at cannulation, the artery may go into spasm. Sometimes, there may be hematoma formation. It is advisable to change the site for arterial line placement at this point. One can use USG currently to improve success at cannulation without complication.

After cannulation, pressure is given on the artery proximal to the catheter tip to reduce bleeding while the pressure transuding assembly is connected.

Step 9: Check Perfusion and Secure the Catheter

- Immediately after cannulation, check perfusion of the extremity. This should also be checked periodically when the arterial catheter is in place.
- Great care should be taken to make sure the catheter stays in place. Although there are various ways of fixing the catheter with adhesive tape, the best method of securing it is to suture it in place. A moderate-diameter, nonabsorbable suture material can be used.
- Place a sterile transparent dressing over the catheter to secure and allow frequent assessment of the catheter insertion site. Label and date the arterial line (Fig. 42.3).
- The arterial line should be connected to a pressure transducing assembly or to an arterial connector when the arterial line is not transduced. This will prevent the line from getting blocked (Fig. 42.3).

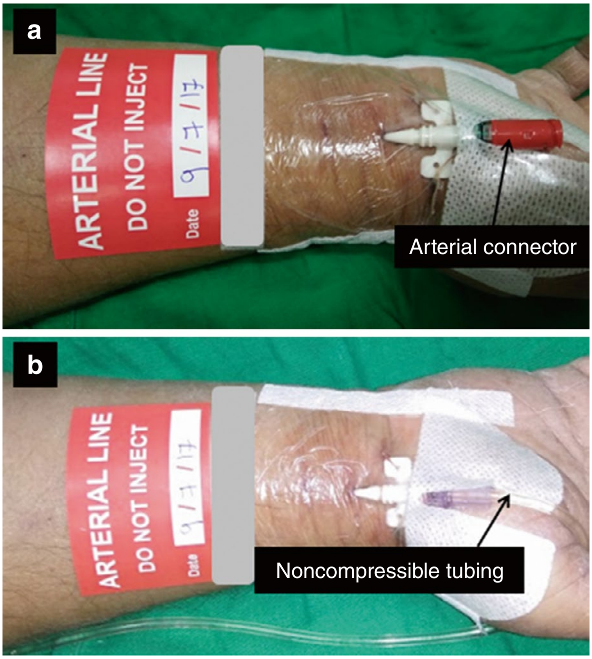
a
ARTERIAL LINE
DO NOT INJECT
Date
9/7/17
Arterial connector
b
ARTERIAL LINE
DO NOT INJECT
Date
9/7/17
Noncompressible tubing

Fig. 42.3 Arterial catheter secured with a sterile transparent dressing and connected to (**a**) an arterial connector (when not transduced) and (**b**) a pressure transducing tubing (when transduced)

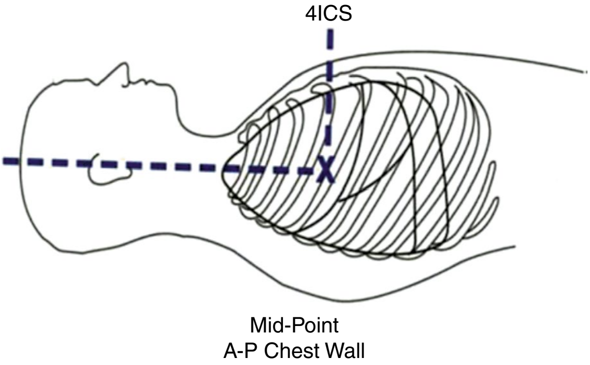
4ICS
Mid-Point
A-P Chest Wall

Fig. 42.4 Phlebostatic axis

Step 10: Zero and Level the Transducer (Static Calibration)

- To obtain accurate pressure measurements, the air–fluid interface must be aligned with the chamber or vessel being measured.
- The reference point is usually at the level of the heart. Use the phlebostatic axis (junction of the fourth intercostal space and midpoint between the anterior and posterior chest walls—Fig. 42.4).
- A spirit level should be used to level this point with the stopcock of the pressure transducing system, which is used for zeroing.

- The transducer is opened to air and the recorded pressure (atmospheric pressure) is used by convention as 0 mmHg reference value.

Step 11: Check If the System Is Optimally Damped (Dynamic Calibration)

- Damping indicates the tendency of an oscillating system to return to its resting state. Anything that takes energy out of the system results in a progressive diminution of amplitude of oscillations.
- *Underdamped waveforms* (will be narrow and peaked tracing and will record higher systolic and lower diastolic pressure) are seen when long tubing is used or with increased vascular resistance.
- *Overdamped waveforms* (will record lower systolic and higher diastolic pressure) are commonly seen when there are air bubbles or blood clots, overly compliant tubing, catheter kinks, stopcocks, no fluid in the flush bag, or low flush bag pressure.
- In both above-mentioned waveforms, the mean arterial pressure (MAP) will not change. Hence, always rely on the MAP, especially when you are not sure whether the system is optimally damped.
- Damping can be checked by doing a "square wave test" (Fig. 42.5). Activate the flush device, quickly release it, and observe the waveform on the monitor. The

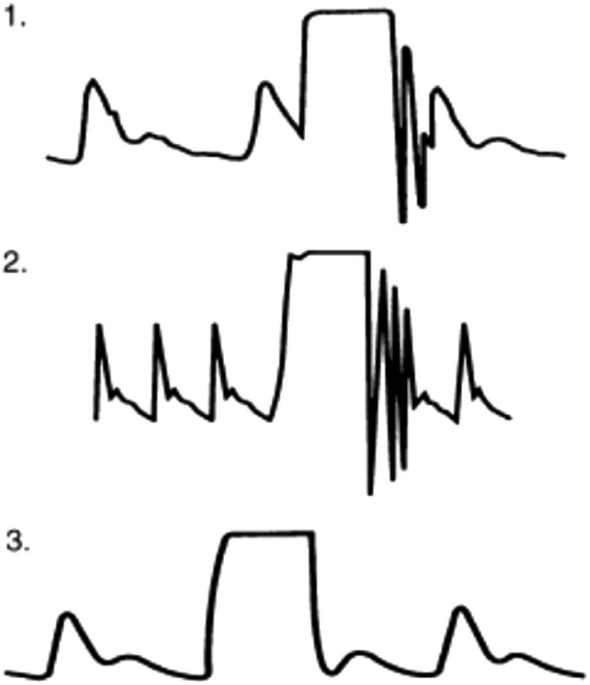

Fig. 42.5 Square wave test

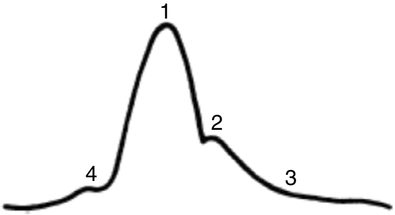

Fig. 42.6 Components of the arterial waveform (*1*—peak systolic pressure, *2*—dicrotic notch, *3*—diastolic pressure, and *4*—anacrotic notch)

waveform will sharply rise and "square off" at the top when the flush is activated and then the tracing returns to the baseline after it is released (Fig. 42.5). Check the number of oscillations.

1. Optimally damped—one or two oscillations before return to tracing
2. Underdamped—more than two oscillations before return to tracing
3. Overdamped—less than one oscillation before return to tracing

Repeat the square wave test every 8–12 h whenever the waveform looks over- or underdamped, when the accuracy of the measurement is doubtful, especially when you are implementing some interventions based on intra-arterial pressure values.

Step 12: Check the Arterial Waveform and MAP (Fig. 42.6)

- Arterial pressure waveforms differ from site to site. As the arterial pressure is recorded more distally, the trace gets progressively more peaked and the dicrotic notch migrates away from the peak as a result of reflected waves in the branching vessels and the decreased arterial compliance of the distributing arteries. The MAP, however, does not vary widely as one measures more distally.
- An under- or overdamped tracing can either under- or overestimate the systolic and diastolic pressures. However, the MAP always remains the same.
- Considering the above, always rely on the MAP, rather than the systolic or diastolic pressure recorded during intra-arterial blood pressure monitoring and titrating therapy.

Step 13: Make Other Interpretations from the Arterial Waveform

Besides more accurate and real-time recording of arterial pressure, a lot of hemodynamic interpretations can be made from the arterial waveform:

- Large variations in pulse pressure (swing in the waveform during mechanical ventilation) can be seen in fluid responsive patients and is used to calculate the pulse pressure variation (PPV) using the arterial waveform analysis. PPV is a dynamic variable to assess fluid responsiveness.

- A steep slope of upstroke means good contractility and vice versa.
- The area under the curve represents the stroke volume.
- Position of the dicrotic notch—low (low systemic vascular resistance) and high (high afterload).
- Slope of the decent—steep (low systemic vascular resistance).

Step 14: Optimize the Natural Frequency of the System to Improve Accuracy

- Use a wide-bore, high-pressure tubing no longer than 122 cm (48 in.).
- Avoid tubing extensions and stopcocks.
- All connections should be tight.
- Eliminate air bubbles.
- Ensure that the flush bag external pressure is 300 mmHg.
- Keep cannulated extremity in neutral or slightly extended position.

Step 15: Ensure Proper Maintenance of the Arterial Catheter

- Ensure that the catheter is always labeled and bears an insertion date.
- Maintain the pressure in the saline bag at 300 mmHg, low pressure reduces the saline flush rate and leads to blockage of catheter with a blood clot and overdamped arterial waveform.
- Check perfusion of the extremity at regular intervals.
- Check the insertion site daily through the transparent dressing for signs of inflammation and infection.
- Change the arterial line dressing only if it is not well coated, very dirty, or there is a collection under it.
- Whenever the arterial catheter is not being transduced, block it using an arterial connector (not a venous connector/stopcock). These color-coded (red) connectors provide high resistance to the blood flow into the catheter, unlike the venous connectors and prevent them from getting blocked. They have a diaphragm through which blood can be collected without removing the connector.
- Special attention should be given while mobilizing and nursing the patient or when a patient is restless, during which the arterial catheter may get accidentally dislodged. An arterial wrist support may be used to prevent such a catastrophe.

Step 16: Watch for Complications

- *Vascular complications* of clinical significance are rare but can be devastating. Attention to the adequacy of distal perfusion is of great importance.
- Absent pulse, dampened waveform, blanched or mottled skin, delayed capillary refill, and painful and cold hands or fingers with motor weakness are presentations of hand ischemia.

- *Infections complications*: Arterial catheters can be responsible for both local and catheter-related bloodstream infections, though the incidence is low. The arterial catheter should be given the same degree of importance as the central venous catheter as a potential source of sepsis. Remove the catheter if it is suspected to be the cause of infection.
- Bleeding, hematoma.
- Nerve damage.
- Pseudoaneurysm.

Step 17: Treat Ischemic Complications If They Occur

- Administering local anesthesia, achieving mild to moderate sedation, and providing a warm environment are interventions that reduce patient anxiety, discomfort, and thus radial artery spasm.
- Black/blue discoloration of fingers—remove the cannula.
- Treatment should be individualized to the patient and expert opinion should be taken early.
- Monitor patient's vital parameters.
- If the patient is on vasopressors, taper the dose if possible.
- If the patient's condition is medically stable, consider the following:
- Arterial duplex sonography
- Angiography
- Patients with symptomatic vasospasm and thrombosis may be treated with topical or intra-arterial vasodilator (nitroglycerin, papaverine, and lidocaine) and anticoagulation therapy. It is advisable to involve a vascular surgeon and interventional radiologist in such cases for expert management.
- If gangrene sets in, it is imperative to involve a vascular and reconstructive surgeon early in the course for operative interventions (thrombectomy and vein grafting for the defect in the involved arterial segment/amputation).

Step 18: Remove the Arterial Catheter at the Earliest

There is no fixed number of days after which the arterial catheter should be removed. Catheter colonization increases with dwell time. Hence, assess the need for the arterial catheter daily and remove it as soon as it is no longer required or earlier if there are any complications.

Suggested Reading

Brzezinski M, Luisetti T, London MJ. Radial artery cannulation: a comprehensive review of recent anatomic and physiologic investigations. Anesth Analg. 2009;109(6):1763–81. *Consistent anatomic accessibility, ease of cannulation, and a low rate of complications have made the radial artery the preferred site for arterial cannulation. Radial artery catheterization is a relatively safe procedure with an incidence of permanent ischemic complications of 0.09%.*

Chaparro Mendoza K. Radial artery catheterism for invasive monitoring: preventing complications, a challenge in anesthesia. Rev Colomb Anestesiol. 2012;40(4):262–5. *Permanent ischemic hand injuries have been reported to occur in 0.09% of cases. A current theory is that an embolic phenomenon that compromises collateral circulation or the digital arteries could be the cause of distal ischemia and residual injuries in surgical interventions. In case this complication appeared, the catheter should be removed and patients with symptomatic vasospasm and thrombosis should be treated with vasodilation and anticoagulation therapy.*

Del Cotillo M, Grane N, Llavore M, Quintana S. Heparinized solution vs. saline solution in the maintenance of arterial catheters: a double blind randomized clinical trial. Intensive Care Med. 2008;34:339–43. *The use of heparinized solution for arterial catheter maintenance does not seem to be justified as it did not increase the duration of the catheters, nor did it improve their functionality significantly. On the other hand, heparin Na altered aPTT significantly.*

Gu WJ, Wu XD, Wang F, Ma ZL, Gu XP. Ultrasound guidance facilitates radial artery catheterization: a meta-analysis with trial sequential analysis of randomized controlled trials. CHEST J. 2016;149(1):166–79. *The use of dynamic 2-D ultrasound guidance for radial artery catheterization decreases first-attempt failure, mean attempts to success, mean time to success, and the occurrence of hematoma complications. Dynamic 2-D ultrasound guidance is recommended as an adjunct to aid radial arterial catheterization.*

Hoste EA, Roels NR, Decruyenaere JM, Colardyn FA. Significant increase of activated partial thromboplastin time by heparinization of the radial artery catheter flush solution with a closed arterial catheter system. Crit Care Med. 2002;30:1030–4. *A heparinized flush solution for the arterial catheter, when used together with a closed-loop blood sampling system, leads to erroneous results of heparin-sensitive coagulation studies*.

Koh DB, Gowardman JR, Rickard CM, Robertson IK, Brown A. Prospective study of peripheral arterial catheter infection and comparison with concurrently sited central venous catheters. Crit Care Med. 2008;36(2):397–402. *In this study, arterial catheter colonization and rates of catheter-related bloodstream infection were found similar to those in concurrently sited and identically managed central venous catheters. By inference, the arterial catheter should be given the same degree of importance as the central venous catheter as a potential source of sepsis.*

Mason PJ, Shah B, Tamis-Holland JE, Bittl JA, Cohen MG, Safirstein J, Drachman DE, Valle JA, Rhodes D, Gilchrist IC, American Heart Association Interventional Cardiovascular Care Committee of the Council on Clinical Cardiology; Council on Cardiovascular and Stroke Nursing; Council on Peripheral Vascular Disease; and Council on Genomic and Precision Medicine. An Update on radial artery access and best practices for Transradial Coronary Angiography and Intervention in Acute Coronary Syndrome: a Scientific Statement from the American Heart Association. Circ Cardiovasc Interv. 2018;11(9):e000035. *This article provides an update on transradial artery access technique and best practices.*

Morelli A, De Backer D. The ten principles behind arterial pressure. Intensive Care Med. 2017;44:1–4. *An update in ICM, about arterial pressure monitoring. The assessment of the arterial pressure values must be interpreted in light of its relationship to cardiac output*.

Saugel B, Kouz K, Meidert AS, Schulte-Uentrop L, Romagnoli S. Correction to: how to measure blood pressure using an arterial catheter: a systematic 5-step approach. Crit Care. 2020;24(1):374. *This article discusses how to place an arterial catheter, correctly measure BP, and identify and solve common pitfalls using a simple five-step approach.*

Wallach SG. Cannulation injury of the radial artery: diagnosis and treatment. Algorithm Am J Crit Care. 2004;13(4):315–9. *Cannulation of the radial artery can result in complications ranging from arterial thrombosis, arterial aneurysm, compartment syndrome, infection, nerve injury, and skin necrosis to possible thumb or even hand necrosis if not recognized and treated early.*

Pulmonary Artery Catheterization

43

Rajesh Chawla, Jaydeep Anadkat, and Aakanksha Chawla

Case Vignette

A 65-year-old male patient, a known case of chronic obstructive pulmonary disease with cor-pulmonale, hypertension, and coronary artery disease with chronic congestive heart failure, was admitted to the ICU with right lower lobe pneumonia. He was in respiratory failure and shock. On the second day, he developed renal failure and azotemia. A pulmonary arterial catheter (PAC) was inserted.

After its inception in the 1970s, pulmonary artery catheterization (PAC) provides direct pressure measurements from the right atrium, right ventricle, pulmonary artery, and pulmonary artery occlusion pressure considered the gold standard in hemodynamic monitoring. It is also a means of measuring cardiac output and mixed venous oxygen saturation. Routine use of this should be avoided, but it still has a role in expert hands in cardiac surgery, difficult-to-treat heart failure, congenital heart disease, complex fluid management situations, and liver transplant surgeries.

Despite all the advantages of PA catheters, several clinical studies have been published in the past 25 years that have shown either no benefit or an increased risk of morbidity or mortality associated with its use.

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Step 1: Assess the Need for PAC—Indications

- PAC is used in situations where right-sided pressures (i.e., central venous pressure [CVP]) may not reflect the changes in pressures in the left side of the heart. Right-sided filling pressures are disproportionately elevated compared to left-sided filling pressures.
- PAC should be used in centers with nursing expertise in the management of catheters and sufficient physician experience in the interpretation of data in the following conditions:
  - Diagnosis of differentiation among causes of shock (cardiogenic, hypovolemic, distributive, obstructive)
  - Management of complicated myocardial infarction
  - For management of heart failure
  - Patients with refractory shock not responding to noninvasive management
  - Patients with significant azotemia on diuretic therapy and are clinically volume-overloaded
  - As part of workup or bridge to cardiac transplant or the left ventricular assist device
  - Complex fluid management (burns, acute renal failure, major surgery) in patients with poor left or right ventricular function
  - Cardiac surgery patients on cardiopulmonary bypass or patients with complex cardiac lesions
  - High-risk obstetric cases such as severe preeclampsia and abruptio placentae
  - Surgical procedures such as liver transplant and aortic cross-clamping

Step 2: Check for the Contraindications

Absolute contraindications:

- Infection at the insertion site
- The presence of a right ventricular assist device
- Lack of consent

Relative contraindications are as follows:

- Complete left bundle branch block may convert to complete heart block.
- Wolff–Parkinson–White syndrome and Ebstein's malformation because of possible tachyarrhythmias. A catheter with pacing capability is preferred in these situations.
- Coagulopathy.
- Severe pulmonary hypertension.
- It should not be used in centers that do not have experience and expertise in its use.

Step 3: Know the PAC

- Circumference should be 7–9 Fr. Most commonly used external diameter is 5 or 7 French (Fr) (1 Fr = 0.0335 mm).
- Length is 110 cm, marked at 10 cm intervals.
- The distal port (yellow colored) at the catheter tip is used for monitoring of pulmonary artery pressure.
- The second port (blue colored) is 30 cm proximal from the tip and is used for monitoring of CVP and injecting fluid bolus for computing cardiac output with bolus technique.
- The third lumen (red colored) leads to a balloon near the tip, with a locking port.
- The fourth-lumen houses wire for a temperature thermistor, the end of which lies just proximal to the balloon. This attaches to the interface cable from the cardiac output monitor.
- The continuous cardiac output PAC has a copper thermal filament embedded in the catheter at 30 cm. Once inserted and connected to the monitor, this filament heats up every few seconds, warms blood around it, and the thermistor in the pulmonary artery detects the change in temperature and calculates cardiac output.
- A variety of catheter constructions are available, each designed for a particular clinical application.
- Double lumen catheter—balloon inflation through one lumen and distal opening for intravascular pressure measurement and blood sampling.
- Triple lumen catheter—proximal port terminating 30 cm from tip of catheter, allowing simultaneous measurement of right atrial and PA or occlusion pressures.
- A quadruple-lumen catheter (most commonly used in the ICU) has a lumen containing electrical leads for a thermistor positioned at the catheter surface 4 cm proximal to its tip.
- Five lumen catheters also available (fifth opening 40 cm from tip of catheter, additional access for fluid and medication infusion).
- Several special purpose PA catheter designs are available. Pacing PA catheter incorporates two groups of electrodes on the catheter surface, enabling intracardiac electrocardiographic (ECG) recording or temporary cardiac pacing.
- A five-lumen catheter allows passage of a specially designed 2.4 Fr bipolar pacing electrode (probe) through additional lumen (located 19 cm from catheter tip) and allows emergency temporary intracardiac pacing without the need for a separate central venous puncture. The pacing probe is Teflon coated to allow easy introduction through the pacemaker port lumen; the intracavitary part of the probe is heparin impregnated to reduce risk of thrombus formation.
- Continuous mixed venous oxygen saturation measurement is clinically available with the help of fiberoptic five lumen PA catheter.
- Heated wire technology for continuous CO monitoring has also been described.

The PAC set also contains the following:

- Large-bore introducer sheath with a one-way valve at its outer end and a side arm extension for intravenous access. (The PAC is introduced through the one-way valve. Some sets may not contain this sheath, but is also available separately.)

- Stiff dilator
- Plastic sheath to cover the catheter
- A 1.5-mL syringe for balloon inflation
- Guidewire
- Puncture needles and syringes
- Three ways and connectors
- A disposable knife

Step 4: Obtain Informed Consent

This has been explained in detail in Chap. 41.

Step 5: Select the Appropriate PAC for Insertion

- Select the PAC that is appropriate for that patient.
- Catheters are available, which can perform the following additional functions:
  - An extra venous infusion port.
  - Pacing capability.
  - Continuous mixed venous oximetry: Special fiber-optic PACs can continuously monitor mixed venous oxygen saturation (SvO_2), initially developed as a surrogate for continuous cardiac output.
  - An ejection fraction catheter has a faster thermistor response time so that it can calculate RV ejection fraction in addition to the cardiac output.
  - Continuous cardiac output.

Step 6: Prerequisites

- Establish monitoring of ECG, noninvasive blood pressure, and pulse oximetry.
- Keep ready all emergency medication and transcutaneous pacing equipment.
- Provide sedation in a conscious patient.
- Supply oxygen through the nasal cannula.
- Secure peripheral venous access.
- Assemble the pressure transducer and flush it.
- An assistant is needed who can prepare the set and closely monitor the patient.
- The patient should be in supine position with the head slightly down and turned toward the opposite side.
- Make use of maximum sterile barrier precautions.

Step 7: Choose the Site of Insertion

- Generally, the right internal jugular vein or left subclavian is selected. If a permanent pacemaker is the in-situ, the opposite side is preferred.
- Alternatively, any other site used for central venous cannulation can be selected keeping in mind the distance from the puncture site to the right atrium.
- An extra distance of 5–10 cm from the left internal jugular, 15 cm from the femoral veins, and 30–35 cm from the antecubital veins is required. However, accurate placement rates are lower from these sites.

Step 8: Prepare the Cannulation Set

With maximum sterile precautions, do the following:

- Pass the catheter through the sterile sheet.
- Flush the catheter with heparinized saline.
- Inflate the balloon with 1.5 mL air and check for its shape and any leakage.
- Zero and level the transducer and connect to the saline-filled catheter.
- Place the tip of the catheter at the heart level; pressure on the monitor should read zero.
- Next, raise the catheter tip to 30 cm height; the monitor should show a pressure of 22 mmHg (equivalent to 30 cm H_2O).

Step 9: Insertion of PAC Through Internal Jugular Vein

- Use maximum sterile barrier precautions.
- Apply generous local anesthesia.
- Locate the internal jugular vein preferably under ultrasonography guidance.
- Puncture the vein with the puncture needle.
- Pass the guidewire through the needle and remove the needle.
- Dilate the skin and subcutaneous tissue with the dilator. This is generally done with the dilator loaded inside the introducer sheath. A small incision is often needed.
- Pass the large-bore sheath using the Seldinger technique.
- Confirm placement by aspirating blood, flushing it, and securing it with stitches.
- Introduce the prepared catheter through the introducer up to a distance of 20 cm with the balloon deflated. Note the waveform on the monitor—CVP tracing should be seen.

- Rotate the catheter so that curvature is at the 11 o'clock position from the patient's head end.
- Inflate the balloon gently with 1.5 cc of air and lock it. During pulmonary artery occlusion pressure (PAOP) measurement, if the balloon is left inflated, one may cause a pulmonary infarct.
- Advance slowly and keep looking at the monitor for RV waveform with systolic peaks of 25–35 mmHg. Note that the diastolic pressure is close to zero. This is reached at around 30–35 cm in length.
- If the RV or PA is difficult to enter:
  - Have the patient take deep breath.
  - Raise the head end of the bed or tilt the table to left or right.
  - Flush the PA port with 1–2 mL cold sterile saline so that the catheter becomes stiff.
- Keep inserting further; PA is reached at 40–45 cm. At PA, there is an increase in the diastolic pressure (Fig. 43.1).
- Now advance another 5–10 cm or so very gradually keeping an eye on the monitor to look for wedging. When it is wedged, the waveform becomes similar to that of CVP tracing at a pressure near the PA diastolic pressure. This is the pulmonary artery occlusion pressure PAOP, and it is always lower than the pulmonary artery diastolic pressure (Fig. 43.1).
- Do not advance any further; deflate the balloon.
- Now inflate the balloon with 0.5 cc increments and look for wedging. If it wedges before 1.5 cc, pull the catheter back 3–4 cm. Do not pull with the inflated balloon.
- Fix the catheter at that length. Note the length of the catheter that led to a good PAOP tracing in the case chart. Use a protector sheath if available or fix it on the skin.
- The pressure measured should be an end-expiratory reading and an aggregate of three readings.
- Never keep the PAC wedged continuously; deflate the balloon after taking the readings.
- Measured and derived hemodynamic indices values are mentioned in Tables 43.2 and 43.3.
- Special considerations—non-flow directed catheters can be put in special disease states (RA or RV dilatation, severe PAH, low CO syndrome) with the help of guidewire although high chances of cardiac perforation (must be done under fluoroscopic guidance with experienced personnel).

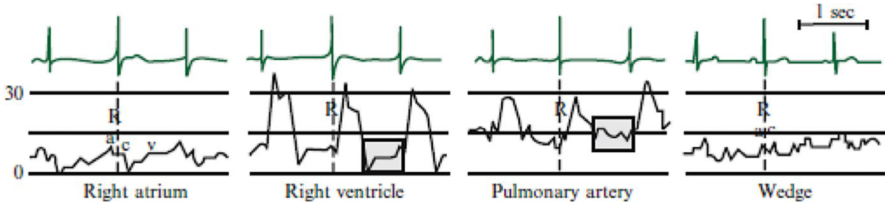

Fig. 43.1 Pressure tracings recorded from the right atrium, right ventricle, pulmonary catheter, and on pulmonary artery occlusion

- Utility of ultrasonography for pulmonary artery catheter insertion is a safe, effective, and fast method of insertion that has an advantage over fluoroscopic guidance. Real-time imaging is done at bedside and does not require patient transport and complex equipment.

Step 10: Manage Complications

- Minor complications are seen in up to 50% of patients, but major complications are seen in only 0.1–0.5% of patients.

Besides all the complications of insertion and maintenance of central venous lines, there are a few unique complications of the use of the PAC (Table 43.1).

Table 43.1 Complications of the PAC

Complication	Description	Treatment
I. Catheterization		
(a) Arrhythmias, ventricular fibrillation	Self-limited arrhythmias extremely common during passage	3.1% of patients require treatment, mostly withdrawal of catheter or guidewire
(b) Right bundle branch block, complete heart block	Transient during passage in 5%	May need transcutaneous or transvenous pacing
	Permanent in 0.9%	
	Should rule out ischemia	
II. Catheter resistance		
(a) Mechanical, catheter knots	Suspect if the catheter is blocked or difficulty in withdrawing	Radiological maneuver
	Confirm on a chest X-ray	Surgery
(b) Thromboembolism	Clots seen within hours	The heparin-coated catheter reduces risk
	Thromboembolism rare	
(c) Pulmonary infarction	Opacity on a chest X-ray	Removal of the catheter
(d) Infection, endocarditis	Significant risk after 72 h, especially in septic patients	Should be removed as soon as feasible
(e) Endocardial damage, cardiac valve injury	53% in autopsy series, but clinically significant regurgitation does not occur	Removal of the catheter
(f) Pulmonary artery rupture	0.02–0.2% of patients, present with hemoptysis and desaturation	One-lung ventilation to isolate normal lung
	Mortality is 50%	Positive end-expiratory pressure to the affected lung
	Cause:	Reverse anticoagulation
	Excessive insertion depth	May try to reinflate to cause tamponade
	Persistent wedging	May need surgical intervention
	Frequent manipulations	
	Inflation with liquid	
(g) Pulmonary artery pseudoaneurysm	Sequelae of PA rupture	Surgery may be needed
	May cause secondary hemorrhage	
III. Misinterpretation of data		May be widespread
		Use requires expertise and experience
IV. Misuse of equipment		

Step 11: Interpretation of Data Obtained (Tables 43.2, 43.3, and 43.4)

Table 43.2 Normal cardiovascular pressures

	Pressures	
	Average (mmHg)	Range (mmHg)
Right ventricle		
Peak systolic	24	15–28
End-diastolic	4	0–8
Pulmonary artery		
Peak systolic	24	15–28
End-diastolic	10	5–16
Mean	16	10–22
Pulmonary artery wedge		
Mean	9	6–15
Left ventricle		
Peak systolic	130	90–140
End-diastolic	7	4–12
Central aorta		
Peak systolic	130	90–140
End-diastolic	70	60–90
Mean	90	70–105

Table 43.3 Derived hemodynamic indices

Parameter	Physiologic significance	Formula	Normal value
Systemic vascular resistance	Reflects impedance of the systemic vasculature	80 × (MAP−CVP)/CO	900–1400 dynes * s/cm^5
Pulmonary vascular resistance	Reflects impedance of pulmonary circuit	80 × (PAM−PCWP)/CO	150–250 dynes * s/cm^2
Cardiac index	Allows for meaningful comparison between patients	CO/BSA	2.8–4.2 L/min/m^2
Stroke volume index	Reflects fluid status and ventricular performance	CI/HR × 1000	30–65 mL/m^2/beat
Left ventricular stroke work index	Estimates work of the left ventricle, reflects contractile state	(MAP − PCWP) × SVI × 0.0136	45–60 gm/m^2
Right ventricular stroke work index	Estimates work done by the right ventricle and RV performance	(PAM − CVP) × SVI × 0.0136	5–10 gm/m^2

CI cardiac index, *CO* cardiac output, *CVP* central venous pressure, *HR* heart rate, *MAP* mean arterial pressure, *PAM* pulmonary artery mean pressure, *PCWP* pulmonary capillary wedge pressure, *SVI* stroke volume index

Table 43.4 Oxygen transport parameters

Parameter	Symbol	Formula	Normal value
Mixed venous oxygen saturation	SvO_2	SaO_2—VO_2 / (Q × 1.34 × Hb)	70–75%
Oxygen delivery	DO_2	1.34 × Hb × SaO_2 × CO	520–570 mL/min/m^2
Oxygen uptake	VO_2	1.34 × Hb × (SaO_2 − SvO_2) × CO	110–160 mL/min/m^2
The oxygen–extraction ratio	O_2ER	VO_2/DO_2	20–30%

Measuring Cardiac Output

- Enter the catheter constant into the monitor; this is generally written on the pack of the set or the insert.
- 10 mL of cold or room temperature saline is smoothly injected from the proximal (blue) port in the right atrium. In small children or patients with volume overload, smaller volumes (2 and 5 mL) may be used.
- A cable from the cardiac output monitor is dipped into the same bottle of saline from which the injectant volume was aspirated.
- The temperature of the blood mixed and cooled with the cold saline is measured at the end of the catheter by a thermistor.
- This produces a thermodilution curve, from which the cardiac output is calculated by the monitor. Usually, three measurements are made.
- These measurements may have a variability of up to 10%.
- Various factors influence the accuracy including intracardiac shunts, tricuspid regurgitation, pulmonary valve regurgitation, respiratory cycle influences, and rapid injection of saline.

Continuous Thermodilution Cardiac Output

- Near-continuous cardiac output can be measured by a specially designed pulmonary artery catheter.
- The RV portion of the catheter has a thermal filament that releases a small amount of heat in a pulsatile manner.
- This temperature variation is measured at the tip of the catheter. It has a measurement delay of 5–15 min, but the measurement is quite reliable.
- Acute changes in cardiac output are detected more slowly, but it has the advantage of ease of operation, minimal handling, and reduced risk of fluid overload.

Pulmonary Capillary Wedge Pressure

- Imagine that the vessel in which the pulmonary artery catheter lies is like a tube connected to the left atrium.
- When there is no flow of blood through the tube, the pressure at the tip of the tube will be the same as the pressure at the left atrium. So, we stop the blood flow by inflating the balloon and measure the pressure at the tip of the pulmonary artery catheter and call it the pulmonary capillary wedge pressure (PCWP), but technically the correct term is pulmonary artery occlusion pressure (PAOP) as PCWP is actually lower than PAOP.
- Pulmonary artery diastolic pressure can be used as an alternative to PCWP to measure left ventricular filling pressure, which we assume predicts left ventricular volume.

- Mean PAOP correlates well with left ventricular end-diastolic pressure (LVEDP) provided the patient has a normal mitral valve and normal left ventricular function. In myocardial infarction, conditions with decreased left ventricular compliance (ischemia and left ventricular hypertrophy) and conditions with markedly increased left ventricular filling pressure (e.g., dilated cardiomyopathy), the contribution of atrial contraction to left ventricular filling is increased. Thus, the LVEDP may be significantly higher than the mean left atrial pressure or PAOP.

Checklist to Follow Before PCWP Can Reliably Reflect the LV Filling Pressure (Table 43.5)

- The tip of the PAC should be in west zone 3 in the lung. The airway pressure fluctuations are minimal in this zone. On the chest X-ray, the tip of the PAC should be below the level of the left atrium within 2 cm of the cardiac silhouette.
- *Correct pulmonary artery and wedge pressure waveforms*: Pulmonary artery pressure upstroke slightly precedes the radial artery pressure upstroke.
- *Rule out abnormal waveforms*: There should be no air, clots, or motion-related artifacts (distinguished from normal by their shape and timing). If the balloon is overinflated and occludes the lumen orifice or forces the catheter tip against the vessel wall—or if there is distal catheter migration—over-wedging may result. Over-wedged pressure is devoid of pulsatility and is higher than expected.
- Measure the pressures only at end-expiration. This is because end-expiratory pressure is closest to the atmospheric pressure. This is done by freezing the waveform on the monitor and observing the movement of the trace up or down along with the phases of respiration or on a paper printout.
- Wedge pressure will underestimate the left ventricular end-diastolic pressure if the patient has diastolic dysfunction, aortic regurgitation, pulmonary regurgitation, right bundle branch block, or postpneumonectomy.
- Wedge pressure will overestimate the left ventricular end-diastolic pressure if the patient has pulmonary arterial hypertension, pulmonary veno-occlusive disease, tachycardia, mitral stenosis, or mitral regurgitation.
- Always remember that wedge pressure is a reflection of LV end-diastolic pressure, whereas it is the end-diastolic volume that determines preload. The two measurements may not correlate in up to 58% of measurements.

Table 43.5 Check list for verifying position of pulmonary artery catheter

	Zone 3	Zone 1 or 2
PAOP contour	Atrial waveform seen (A + V waves)	Unnaturally smooth
PAD versus PAOP	PAD > PAOP	PAD < PAOP
Respiratory variation of PAOP	$<1/2\ P_{ALV}$	$\geq \blacktriangle P_{ALV}$
Catheter-tip location	LA level or below	Above LA level

PAD pulmonary artery diastolic pressure

Suggested Reading

American Society of Anesthesiologists Task Force on Pulmonary Artery Catheterization. Practice guidelines for pulmonary artery catheterization: an updated report by the American Society of Anesthesiologists Task Force on Pulmonary Artery Catheterization. Anesthesiology. 2003;99:988–1014. *A detailed review of the various aspects of the use of the pulmonary artery catheter along with recommendations and practice guidelines on its management and use.*

Connors AF Jr, Speroff T, Dawson NV, et al. The effectiveness of right heart catheterization in the initial care of critically ill patients. SUPPORT Investigators. JAMA. 1996;276(11):889–97. *PAC use was associated with increased mortality and increased utilization of resources. Subgroup analysis did not reveal any patient group or site for which the PAC was associated with improved outcomes. This study started the outcome controversies on PAC use*.

Hofer RE, Vogt MNP, Taner T, et al. Influence of intraoperative transesophageal echocardiography and pulmonary artery catheter monitoring on outcomes in liver transplantation. Transplant Direct. 2020;6:e525. *Compared with either TEE alone or PAC alone, intraoperative monitoring with TEE + PAC during OLT was associated with the shortest length of hospitalization and lowest 30-day mortality rate. Transplant anesthesiologists should be aware of the potential benefit on patient mortality and hospital length of stay with concurrent intraoperative TEE + PAC monitoring and the increased need for new postoperative dialysis.*

Kadosh BS, Berg DD, Bohula EA, et al. Pulmonary artery catheter use and mortality in the Cardiac Intensive Care Unit. JACC: Heart Fail. 2023;11(8):903. There is wide variation in the use of PACs that is not fully explained by patient level-factors and appears driven in part by institutional tendency. *PAC use was associated with higher survival in cardiac patients with shock presenting to CICUs.*

Swan HJC, Ganz W, Forrester JS, Marcus H, Diamond G, Chonette D. Catheterization of the heart in man with use of a flow-directed balloon-tipped catheter. N Engl J Med. 1970;283:447–51. *The landmark article that completely changed the way people monitored patients in the ICUs. Since its introduction the catheter has hardly undergone change in size or structure. It was at one time the most widely used equipment in the ICU*.

Defibrillation and Cardioversion

44

Rajesh Chawla, Tatineni Venu Gopal, Jagan Prashanth,
and Pradeep Jain

Case Vignette

A 70-year-old diabetic, hypertensive, and coronary artery disease male patient was admitted to the hospital with acute myocardial infarction. His pulse was 120/min, and his blood pressure was 100/60 mmHg. He was on Noradrenaline and dobutamine infusion. He was being prepared for primary angioplasty. While being shifted to the catheterization laboratory, he collapsed. The cardiac monitor showed ventricular fibrillation (VF).

Electrical cardioversion and defibrillation have become routine procedures in the ICU in the management of arrhythmia. Reentry is the predominant mechanism of majorities of arrhythmias in ICUs. Electrical shock therapies are capable of terminating arrhythmias due to reentry.

Cardioversion is the delivery of energy that is synchronized to the QRS complex, while defibrillation is the non-synchronized delivery of a shock randomly during the cardiac cycle.

Cardioversion terminates arrhythmias by delivering a synchronized shock that depolarizes the tissue involved in a reentry circuit. All excitable tissue of the circuit are depolarized and makes the tissue refractory. The circuit is not able to propagate or sustain reentry. So, cardioversion terminates those arrhythmias resulting from a

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single reentry circuit, such as atrial flutter, atrioventricular nodal reentrant tachycardia, atrioventricular reentrant tachycardia, or monomorphic ventricular tachycardia.

Step 1: Be Familiar with the Device

- *Types of defibrillators*
  - Manual external defibrillators (Fig. 44.1)

    These defibrillators have electrocardiogram (ECG) readers, which the health care provider uses to diagnose a cardiac rhythm. The health care provider will then decide what charge (in joules) to use, based on proven guidelines (ACLS) and experience, and will deliver the shock through paddles or pads on the patient's chest.

    As they require detailed medical knowledge, these units are generally only found in hospitals and on some ambulances.
  - Automated external defibrillators (AEDs) (Fig. 44.2).

    AEDs are sophisticated, reliable computerized devices that use voice and visual prompt to guide lay users and health care providers to safely defibrillate the appropriate rhythm.

Fig. 44.1 Defibrillator

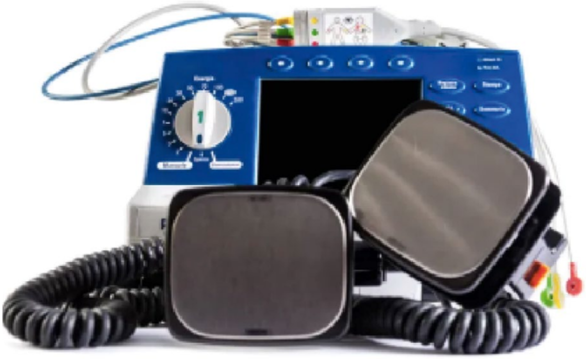
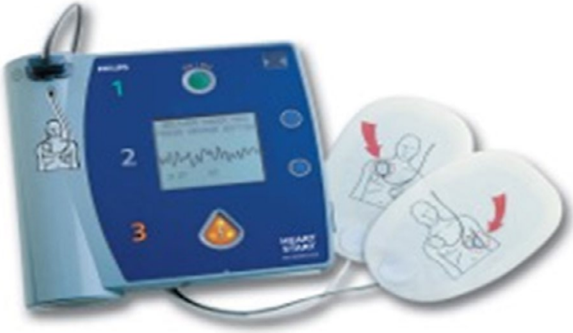


Fig. 44.2 AED



    They are not designed to deliver synchronized shock (i.e., cardioversion of ventricular tachycardia (VT) with pulse). They will rather recommend a non-synchronized shock for both monomorphic and polymorphic VTs if the rate and morphology exceed the preset value.

    If a victim has chest hair, check the AED for a razor or second set of pads. Ensuring proper contact with the patient's chest for effective AED use is important. If a razor is available, shave the chest areas to allow the pads to stick. If no razor is present, but a second set of pads is, take the first set of pads and place them onto the victim. Then forcibly remove the pads, ripping the hair from the chest. Now the second pad can be used without interference.

    The AEDs take time (~10–20 s) to diagnose the rhythm. On the other hand, a professional can diagnose and treat the condition far more quickly with a manual unit. This valuable time gap between analysis and application of shock, where the chest compression must be withheld, is unavoidable for the AEDs.

    These time intervals for analysis, which require stopping chest compressions, have been shown in several studies to have a significant negative effect on shock success. This effect led to the change in the AHA defibrillation guideline (calling for 2 min of cardiopulmonary resuscitation (CPR) after each shock without analyzing the cardiac rhythm), and some recommend that AEDs should not be used when manual defibrillators and trained operators are available.

    There are two types of AEDs: fully automated and semiautomated. Most AEDs are semiautomated. A semiautomated AED automatically diagnoses heart rhythms and determines if a shock is necessary. If a shock is advised, the user must then push a button to administer the shock.

    A fully automated AED automatically diagnoses the heart rhythm and advises the user to stand back while the shock is automatically given. Also, some types of AEDs come with advanced features, such as a manual override or an ECG display.

  - Implantable cardioverter defibrillators (ICD)

    ICDs analyze the rhythm based on an internal program and shocks appropriately.

- *Types of shocks*
  - *Monophasic*

    A monophasic shock delivers current in one polarity.

  - *Biphasic shocks*

    A biphasic shock delivers a current that reverses course during the pulse.

    Defibrillation with biphasic waveform improves short-term outcome of terminating ventricular fibrillation (VF).

    It is safe and has equivalent or higher efficacy in terminating VF than the monophasic.

    Recommendation is 120–200 J according to manufacturer's recommendation. If not known, then defibrillate at the maximum dose.

Nowadays biphasic defibrillators have largely replaced monophasic in most of the institutions.

Dual sequence defibrillation (DSD)

- Two defibrillators are used to increase the amount and direction of energy transmitted through the chest on the same patient, at the same time.
- The first pad should be placed immediately medial or lateral to the pad located at the right sternal border without touching the first pad. The second pad should also be placed medial or lateral to the first defibrillator pad located at the cardiac apex not touching each other or anterior–posterior placement of the second set of defibrillator pads is also an option.
- In the DOSE VF study, survival to hospital discharge appeared higher with DSD and VC (vector change) in refractory VF.

The Modes (Defibrillation and Cardioversion)

- *Defibrillation*

  Defibrillation is a method of introduction of unsynchronized electrical shock that stuns the heart briefly and terminates all electrical activities including VF and rapid VT, and if the heart is still viable then its pacemakers will eventually resume its normal rhythm, which ultimately results in a perfusing rhythm. It is not synchronized with the R wave in ECG.
- *Cardioversion*

  Here, the shock delivery is synchronized with QRS complexes. It prevents shock delivery during the relative refractory portion of the cardiac cycle (i.e., ventricular vulnerable period, between 60 and 80 ms before and 20–30 ms after peak of the T wave) when shock could produce VF.
- *Electrodes*
  - *Types*

    Handheld paddles (pediatric and adult)

    Self-adhesive pads (pediatric and adult)
  - *Size*

    8–12 cm for the adult and child (≥8 years)

Step 2: Assess the Need for Cardioversion and Defibrillation—Indications and Contraindications (Tables 44.1, 44.2, and 44.3)

- Electrical cardioversion is most effective in terminating tachycardias related to reentry, such as atrial flutter and many cases of AF, AV node reentry, reciprocating tachycardias associated with WPW syndrome, most forms of VT, ventricular flutter, and VF. The electrical shock, by depolarizing all excitable myocardium and possibly by prolonging refractoriness, interrupts reentrant circuits and establishes electrical homogeneity, which terminates reentry.

Table 44.1 Indication of cardioversion and defibrillation

Type	Indications
Immediate	Hemodynamic instability due to tachyarrhythmia of shockable variety
	Congestive heart failure and angina due to shockable tachyarrhythmia
Elective	Hemodynamically stable
	No significant symptoms

Table 44.2 Tachyarrhythmias responsive to electrical therapy

Responsive to cardioversion		Responsive to defibrillation
Supraventricular	Ventricular	Pulseless VT
		VF
Atrial fibrillation	Monomorphic VT with pulse	Unstable polymorphic VT with or without pulse
Atrial flutter		
Sinoatrial nodal reentrant tachycardia		
Atrioventricular nodal reentrant tachycardia		
Atrioventricular reciprocating tachycardia		

Table 44.3 Tachyarrhythmias unresponsive to electrical therapy

Unresponsive to cardioversion/defibrillation	
Supraventricular	Ventricular
Sinus tachycardia	Idiopathic monomorphic VT
Multifocal atrial tachycardia	
Junctional tachycardia	Accelerated idioventricular rhythm

- If the precipitating factors are no longer present, interruption of the tachyarrhythmia for only the brief time produced by the shock may prevent its return for long periods, even though the anatomic and electrophysiologic substrates required for the tachycardia are still present.
- Tachycardias thought to be caused by disorders of impulse formation *(automaticity)* include parasystole, some forms of AT, junctional tachycardia (with or without digitalis toxicity), accelerated idioventricular rhythm, and relatively uncommon forms of VT. An attempt to cardiovert these tachycardias electrically is not indicated in most cases because they typically recur within seconds after the shock, and the release of endogenous catecholamines consequent to the shock can perpetuate the arrhythmia. It has not been established whether cardioversion can terminate tachycardias caused by enhanced automaticity or triggered activity.

Caution: Patients with digitalis toxicity, electrolyte imbalance (more prone to ventricular fibrillation (VF) and ventricular tachycardia (VT) aftershock), chronic atrial fibrillation (AF), and atrial flutter (AFL) of more than 48 h who are not adequately anticoagulated.

Step 3.1: Method for Cardioversion

- *Patient preparation for elective cardioversion*
  - It should be done in hospital areas equipped with cardiac monitoring, airway management, and cardiopulmonary resuscitation.
  - Ensure nil by mouth (NBM) status.
  - Patient counseling is required in detail about the procedure.
  - Obtain valid informed consent from the patient or legal surrogate.
  - Confirm adequacy of anticoagulation in chronic AF.
  - Consider starting antiarrhythmics 24–48 h pre-procedure.
  - Pre- and postprocedure ECG.
- *Preprocedural sedation protocol*
  - If the patient requires oxygen or is currently receiving oxygen, oxygen tubings should be kept away from the chest.
  - Continuous monitoring—ECG, SPO_2, and noninvasive blood pressure (NIBP).
- *Give sedation and analgesia.*
  - Agents—propofol, midazolam, and etomidate.
  - Propofol is the best option for its early awakening time and better safety profile. Short-acting agents are preferred.
  - Opioid analgesics, such as fentanyl, are used for analgesia.
- *Conscious sedation*
  - Goal—maintain consciousness but in a somnolent state. It can be done by a trained physician without anesthesiologist’s supervision. Midazolam is the preferred agent here.
- Turn the defibrillator on (monophasic or biphasic shock)

  It simultaneously switches the monitor on.

- *Suggested electrode position* (Figs. 44.3 and 44.4)
  - Anterolateral (most common): An anterior paddle is placed in the right infraclavicular area, and the lateral paddle is placed lateral to the left breast in longitudinal alignment.
  - Anteroposterior: The anterior paddle is the same as before, and the posterior paddle is on the left side of the spine at the level of the lower end of the scapula.
  - Other two positions, include anterior-left infrascapular and anterior-right infrascapular. Anteroposterior placement is found to be more successful in cardioversion of AF with monophasic shock.
  - Apply jelly (water-based conducting jelly). Place the negative electrode closer to the heart with both electrodes adequately separated.
  - The conducting jelly should be restricted to the pad area and should not be spread all over the chest to prevent superficial transferring of current.
- *Synchronization (for synchronized cardioversion)*
  - The device should be in the synchronized mode as most have a default unsynchronized mode.

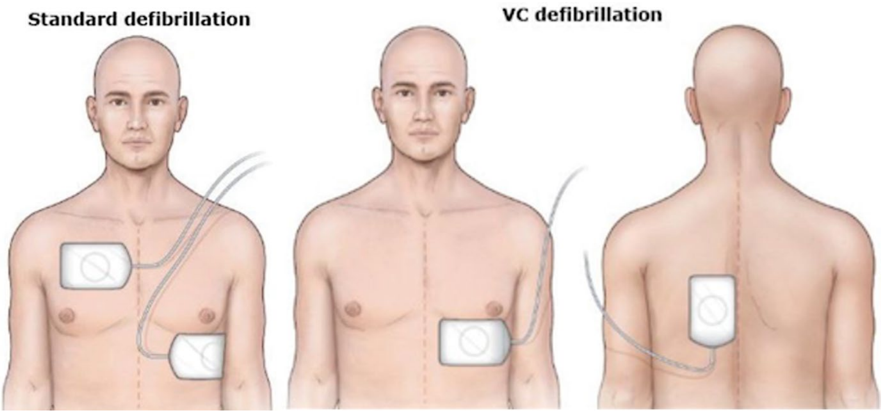


Fig. 44.3 Position of paddle placement in standard defibrillation, vector change (VC) defibrillation

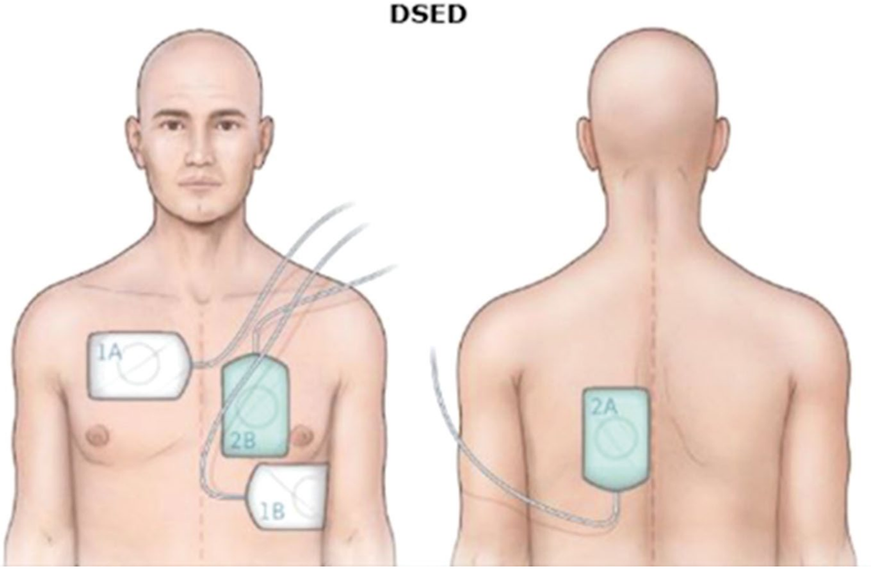


Fig. 44.4 Position of paddle placement in dual sequence defibrillation (DSD)

- For each subsequent defibrillation, one needs to reset to synchronized mode. Confirm synchronization by looking at markers on the R wave. It may be necessary to adjust the gain of the monitor to remark the R wave correctly.
- Announce “charging-stand clear”
- Charge

Press the charge button (present on the paddle as well as on the monitor) to select the level of charge (Table 44.4). Hear the audible sound/alarm when charging is completed (Fig. 44.5).

Table 44.4 Specific energy levels

Rhythm	Mode	Monophasic (initial and consecutive shocks)	Biphasic shock
VF, pulseless VT	Defibrillation	360	120-200
Stable, monomorphic VT with pulse	Cardioversion	100, 200, 300, 360	70, 120, 150, and 170[a]
AF	Cardioversion	100–200, 300, 360	100–120
Atrial flutter	Cardioversion	50, 100, 200, 300, 360 (MDS)	70, 120, 150, and 170[a]
Supraventricular tachycardia (SVT)			

[a] The biphasic waveform using the lower energy level is acceptable if documented to be clinically equivalent or superior to reports of monophasic shock success. Initial biphasic dose of 100–200 J with escalation depending on the need is recommended (evidence extrapolated from cardioversion of atrial fibrillation). For specific recommendation, consultation from the device, manufacturer is advised

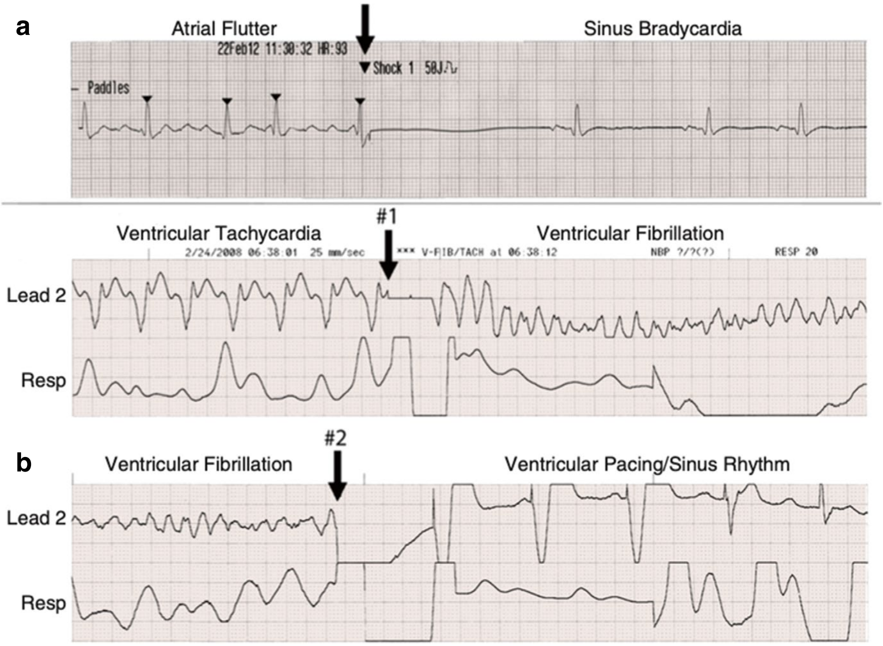

a
Atrial Flutter
22Feb12 11:30:32 HR:93
Shock 1 50J
Paddles
Sinus Bradycardia
Ventricular Tachycardia
2/24/2008 06:38:01 25 mm/sec
#1
*** V-FIB/TACH at 06:38:12
NBP ?/?(?)
RESP 20
Ventricular Fibrillation
Lead 2
Resp
b
Ventricular Fibrillation
#2
Ventricular Pacing/Sinus Rhythm
Lead 2
Resp

Fig. 44.5 Cardioversions. (**a**) Synchronized shock (note the synchronization mark in the apex of the QRS complex, *arrowhead*) during atrial flutter is followed by sinus bradycardia. (**b**) *(top),* Shock (*#1*) is delivered during ventricular tachycardia but asynchronously (on the T wave); this results in ventricular fibrillation, which is then treated with a second, asynchronous shock (*#2*) that results in sinus rhythm with tracked ventricular pacing. *Resp* Respirations

- *Clearing*

  Say “I am going to shock on three; one, I am clear; two, you are clear; three, everybody is clear.” Check and look around after each step and confirm safety.
- *Shock*

  Check to see the synchronized mode prior to giving a synchronized shock.

Step 3.2: Method for Defibrillation

- Analyze the rhythm

  A bedside cardiac monitor or ECG display of the defibrillator is needed, if already attached.
- Sedation protocol

  As most often patients with pulseless VT and VF present in an emergent condition with unstable hemodynamics and impending cardiac arrest, sedation in such cases is not required.
- Turn the defibrillator on

  In most defibrillators, the default mode is the asynchronized mode.
- Same as step D for cardioversion
- No need for synchronization
- Same as cardioversion up to step H
- Shock (asynchronized)
- Post-shock

Resume CPR for five cycles, check rhythm, and proceed according to ACLS guidelines.

Step 4: Manage Complications (Table 44.5)

Table 44.5 Complications and their prevention/treatment

Complications	Prevention/treatment
Thermal burns	The lowest accepted energy level
	Biphasic shock requires less energy
Thromboembolism	More common with AF (incidence in 1–7% patients who are not receiving anticoagulation)
	Ensure adequate anticoagulation
	Exclude left atrial clots with transesophageal echocardiography
Arrhythmia	For expected sinus bradycardia and sinus arrest, prophylactic placement of the pacemaker (transvenous/transcutaneous) in patients with AF with slow ventricular rate
	VT and VF—in patients with digitalis toxicity or hypokalemia, better to avoid cardioversion; if necessary to perform, then be prepared for a more refractory ventricular arrhythmia
Myocardial damage	Clinically insignificant but recommended to give two shocks at least 1 min apart
Loss of airway	Mostly sedation related
	Complications such as aspiration can be reduced by ensuring nil by mouth (in elective cases), supervised cardioversion preferable
Pulmonary edema	Supportive measures and gradual improvement expected
Fire hazard	Reported when shock is given in an oxygen-rich environment
	Avoid direct blowing of oxygen across the chest in the oxygen-rich environment

Step 5: Special Circumstances

- *Anticoagulation for reverting atrial fibrillation and flutter*
  - Anticoagulation is indicated in atrial fibrillation and flutter lasting more than 48–72 h.
  - Recommendation is 3–4 weeks of anticoagulation before attempt cardioversion. It should be continued for at least 4 weeks post-cardioversion.
  - This approach has an inherent risk of increased bleeding. So, in patients at a higher risk of bleeding, transesophageal echocardiography can be performed to exclude intracardiac thrombus and proceed with cardioversion without adequate prior anticoagulation. In any case, at least 4 weeks of anticoagulation is mandatory in the post-cardioversion period.
- *External defibrillation with the ICD/pacemaker in situ (*Fig. 44.6*)*
  - If the ICD is currently delivering shock (as evidenced by external muscle contraction similar to external defibrillation), allow 30–60 s for the ICD to complete the treatment cycle.
  - Position the external defibrillation pads in a clinically acceptable position that is as far from the pulse generator as possible. When a device is located in an area where a pad would normally be placed, the AHA recommends positioning the external defibrillation pad at least 1 inch (2.5 cm) away from the device.
  - It is not desirable to place the pads or paddles directly over the device.
- *Pregnancy*

  Cardioversion and defibrillation have been performed in all trimesters of pregnancy. It has been found to have no obvious adverse fetal effects or premature labor. Fetal heart rhythm monitoring is recommended.
- *Pediatric age group*
  - The lowest energy dose for effective defibrillation is not known. The lower and upper limits to safe defibrillation are not known for infants and children.
  - Biphasic shocks appear to be at least as effective as monophasic shocks and are less harmful than monophasic shocks.
  - It is recommended to use an initial dose of 2–4 J/kg, and for refractory VF, increase the dose to 4 J/kg. Subsequent energy levels should be at least 4 J/kg,

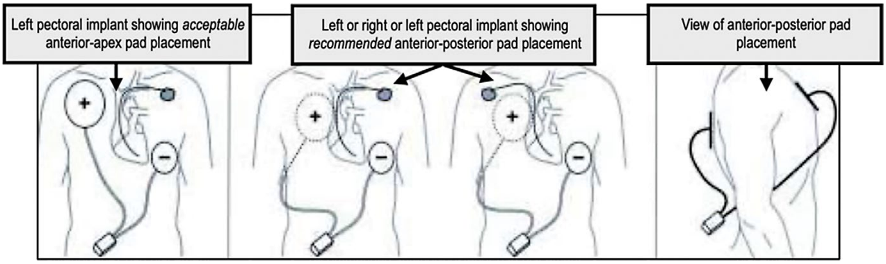

Left pectoral implant showing *acceptable* anterior-apex pad placement
Left or right or left pectoral implant showing *recommended* anterior-posterior pad placement
View of anterior-posterior pad placement
+
−
+
−
+
−

Fig. 44.6 Placement of external defibrillation pads for pacemaker or defibrillator patients

  and higher energy levels may be considered, but not to exceed 10 J/kg or the adult maximum dose.
  - For infants (<1 year of age), a manual defibrillator is preferred. If a manual defibrillator is not available, an AED with pediatric attenuation is desirable. If neither is available, an AED without a dose attenuator may be used.
- *Drowning*
  - Removal of the patient from water and thorough wiping of the chest and the patient is a prerequisite before attempting electrical therapy.
- *Hypothermia*
  - Defibrillation is less effective in hypothermia. For VF/VT without pulse, it is reasonable to attempt defibrillation with a single shock, even in severe hypothermia. Further single attempts can be made with every 1–2 °C increase in core temperature. Above 30 °C, follow ACLS guidelines for normothermia.

Step 6. Remember Factors Affecting Defibrillation and Shock

Equipment related

- *Electrode position*: Anterolateral electrode position is suggested for persons with an underlying cardiac implantable electronic device (CIED) such as a permanent pacemaker or an implantable cardioverter-defibrillator.
- It is recommended to place the external electrode pads in the anteroposterior position to avoid any contact with the skin overlying the cardiac implantable electronic device.
- *Pad size*: A larger pad or paddle surface is associated with a decrease in resistance and increase in current and may cause less myocardial necrosis.
- Use optimal electrode size (approximately 12.8 cm) above which there is decline in current density.
- *Hand-held* versus *patch*: Hand-held paddle electrodes are more effective than self-adhesive patch electrodes, especially for cardioversion of persistent atrial fibrillation. No data is available for other arrhythmia needing cardioversion.
- *Monophasic* versus *biphasic waveforms*: Biphasic waveforms defibrillate more effectively and at lower energies than monophasic waveforms.

Patient related

- *Transthoracic impedance*: It depends on the following factors:
  - Energy level
  - Electrode-to-skin interface
  - Interelectrode distance
  - Electrode pressure (with hand-held electrodes)
  - Phase of ventilation
  - Myocardial tissue and blood conductive properties
- *Types of arrythmia*: The type of arrhythmia and the patient’s clinical condition are important determinants of defibrillation success

- *Duration of arrhythmia*
- *Patients with an underlying cardiac implantable electronic device*

Suggested Reading

Cheskes S, et al. Defibrillation strategies for refractory ventricular fibrillation. NEJM. 2022;387:1947–56.

Field JM, Gonzales L, Hazinski RJ, Talley R, Elling B, et al. Advanced cardiac life support. Dallas: American Heart Association; 2006a. p. 34–8. *AHA guidelines for the management of tachyarrhythmias.*

Field JM, Gonzales L, Hazinski RJ, Talley R, Elling B, et al. Advanced cardiac life support. Dallas: American Heart Association; 2006b. p. 90–5. *AHA guidelines for the management of tachyarrhythmias.*

Fink MP, Abraham E, Vincent JL, Kochanek PM. Textbook of critical care. 5th ed. Philadelphia: Elsevier Sauders; 2005. *This gives a comprehensive description of cardioversion.*

Irwin RS, Rippe JM. Irwin and Rippe's intensive care medicine. 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2008. p. 73–9. *Detailed procedure and indication with pictorial depiction for electrode placement.*

Link MS, Atkins DL, Passman RS, Halperin HR, Samson RA, White RD, Cudnik MT, Berg MD, Kudenchuk PJ, Kerber RE. Electrical therapies. Automated external defibrillators, defibrillation, cardioversion, and pacing. 2010 American Heart Association guidelines for cardiopulmonary resuscitation and emergency cardiovascular care. Circulation. 2010;122(Suppl 3):S706–19. *A recent recommendation and comprehensive review of AHA.*

Temporary Pacemaker Insertion

45

Rajesh Chawla, Vivek Kumar, and Ashutosh Bhardwaj

Case Vignette
A 70-year-old male patient—a case of coronary artery disease on regular treatment—was admitted to the hospital with chief complaints of syncope and giddiness. His heart rate was 38/min and blood pressure was 90/60 mmHg. ECG showed complete heart block. Insertion of temporary pacemaker was planned.

Pacemakers provide electrical stimuli that cause cardiac contraction when the intrinsic myocardial electrical activity is slow or absent. Temporary pacemakers use an external pulse generator with leads placed either transcutaneously or transvenously. During emergency resuscitation, transcutaneous leads are the easiest and most convenient method of choice. Transcutaneous pacing requires mild sedation. For transvenous pacing, a semirigid catheter is placed through central access. ECG monitoring/echocardiography may be used for tracking catheter positioning at bedside. If possible, patient should be shifted to Cathlab for reliable lead positioning.

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Step 1: Assess the Need for the Temporary Pacemaker (Tables 45.1 and 45.2)

Contraindications

For patients especially with life-threatening hemodynamic instability and symptomatic bradyarrhythmias or other indications for temporary cardiac pacing, there are no absolute contraindications.

Temporary transvenous cardiac pacing should be avoided or used with caution in the following settings:

- Intermittent, mild, or rare symptoms in whom the bradycardia is well tolerated.
  - Symptomatic complete heart block with an adequate and "stable" narrow QRS escape rhythm
  - Symptomatic sinus node dysfunction with only rare pauses
- Patients with a prosthetic tricuspid valve, as the temporary cardiac pacemaker lead could damage the valve or become trapped in the prosthesis.
- Patient with an MI who has received a thrombolytic agent and is being aggressively treated with anticoagulation or antiplatelet agents.

Table 45.1 Indications of temporary pacing in the absence of acute myocardial infarction (electrolyte disturbance/drug Toxicity/myocarditis)

Symptomatic bradycardia refractory to medical treatment Sinus node dysfunction Second- or third-degree atrioventricular (AV) block
Third-degree AV block with wide QRS escape or ventricular rate <40 bpm
Prophylactic

Table 45.2 Indications of temporary pacing in acute myocardial infarction

Class I
Asystole
Symptomatic bradycardia (includes sinus bradycardia with hypotension and type I second-degree AV block with hypotension not responsive to atropine)
Bilateral bundle-branch block [BBB; alternating BBB or right BBB (RBBB) with alternating left anterior fascicular block (LAFB)/left posterior fascicular block (LPFB)] (any age)
New bundle-branch block with Mobitz II second-degree AV block
RBBB plus fascicular block with Mobitz II second-degree AV block
Class IIa
Narrow QRS plus Mobitz II second-degree AV block
Old or new fascicular block with Mobitz II second-degree AV block and anterior myocardial infarction
Old bundle-branch block and Mobitz II second-degree AV block
New bundle-branch block plus first-degree AV block
New bundle-branch block plus Mobitz I second-degree AV block
RBBB plus LAFB or LPFB (new or indeterminate) with first-degree AV block
RBBB plus LAFB or LPFB (new or indeterminate) with Mobitz I second-degree AV block

Step 2: Be Familiar with the Device (Table 45.3)

Temporary cardiac pacing techniques—temporary cardiac pacing can be performed in a variety of ways:

Internally using transvenous endocardial leads
Externally via transthoracic patches
Internally using atrial or ventricular epicardial leads placed at the time of surgery
Internally via an esophageal electrode, which is primarily used for atrial pacing and recording

Table 45.3 Temporary pacemaker method and device details

Device	Parts	Current	Benefits	Drawback	Uses
Transcutaneous external pacemakers	External patch electrodes	Higher current (up to 200 mA) and longer pulse duration (20–40 ms)	Less time-consuming	Require sedation	Cardiac arrest
	Pulse generator (usually a defibrillator)		Risks of central venous access avoided	Pacing limited to ventricle and minimal capacity for atrial pacing Failure to pace Skeletal muscle stimulation	Symptomatic bradyarrhythmia Overdrive pacing Prophylactically for arrhythmia in myocardial infarction Unavailability or contraindication to transvenous pacing (prehospital setting during thrombolytic therapy for acute myocardial infarction)
Transvenous pacing	Transvenous pacing catheters (4–7 F)	Threshold for vent	Different modes (ventricular, arterial, sequential)	Inherent risk with central venous line Pericardial tamponade	Indications as per Table 45.1
	Pulse generator	Pacing (<1 mA), atrial pacing (<2 mA) Output three to four times of threshold			

Transcutaneous needle temporary pacemaker should not be used in current technology as it has serious complications

Step 3: Transvenous Pacemaker—Procedure

- *Obtain a central venous access*
  - *The preferred route*: Internal jugular (most common and most preferred), subclavian, and femoral veins, preferably right-sided veins, should be used when possible. Local anesthesia is always indicated.
  - Access blind or ultrasound-guided intracardiac placement of the pacing wire.
- *Intracardiac placement of the pacing wire*
  - This should only be inserted by experienced practitioners.
- Preparation:
  - A defibrillator and other resuscitation equipment should be immediately accessible.
  - Strict aseptic technique.
  - ECG monitoring.
- Cannulate the suitable vein (internal jugular, subclavian, or femoral veins preferably on the right side) using Seldinger's technique of guidewire and dilators to place a sheath of the correct size.
- Bend the tip of the electrode to give a 20–30° curve for the correct positioning in the heart.
- Advance the electrode under ultrasound or fluoroscopic guidance until it lies vertically in the right atrium with its tip pointing toward the free wall on the right side.
- Rotate the wire between the index finger and the thumb so that it points toward the patient's left side; advance the wire steadily through the tricuspid valve and along the floor of the right ventricle to the apex.
- If blind technique is used, the V1 lead is connected to the distal port (cathode). Endocardial contact is indicated by prominent ST-segment elevation. Placement is facilitated by balloon inflation and floatation in the superior vena cava. Position is confirmed by successful capturing. The anteroposterior X-ray after placement is always indicated.
- If AV sequential pacing is desired, the atrial J-shaped pacing catheter should be advanced into the right atrium and rotated anteromedially to achieve a stable position in the right atrial appendage; positioning the atrial catheter usually requires fluoroscopy.
- *Setting the pacemaker*
  - Keep the pacemaker box in off position and attach the leads to the ventricular output position.
  - Turn the pacemaker into asynchronous mode and set the ventricular rate 10–20 beats/min higher than the patient's intrinsic rate.
  - Set the threshold current for ventricular pacing at 5.0 mA and switch the pacemaker on. See for ventricular pacing as evidenced by a wide QRS complex, with ST-segment depression and T-wave inversion, following each pacemaker

depolarization (spike). (Right ventricular apex pacing presents as a pattern of left bundle-branch block on the surface ECG.)

- Output current is slowly reduced and the threshold current (the lowest current at which consistent ventricular capture occurs) is determined. Recommended pacing threshold of less than 0.5–1.0 mA should be achieved.
- If the threshold is high, then consider relative endocardial refractoriness due to fibrosis (rare) or a malposition of the electrode (more common). In any case, the tip of the pacing electrode should be repositioned in the region of the ventricular apex until satisfactory ventricular capture at a current of less than 1.0 mA is consistently maintained.
- The ventricular output is set to exceed the threshold current at least threefold. The pacemaker is now in VOO mode.
- After insertion of the lead and before stitching the lead, withdraw the sheath as it reduces infection rate.

Step 4: Know the Modes (Table 45.4)

Table 45.4 Modes

Modes	Paced (A, atrium; V, ventricle; D, dual)	Sensed (A, atrium; V, ventricle; D, dual)	Response (I, inhibit; T, trigger)	Programmability (R, programmable; O, nonprogrammable; M, multiprogrammable)	Multisite pacing (A, multisite pacing; O, non-multisite pacing)
VVI	Ventricle	Ventricle	A sensed event in the ventricle inhibits the pacemaker from pacing or producing any output	None	None
AAI	Atrium	Atrium	The sensing of an event (e.g., sensing atrial activity within 1 s) inhibits the pacemaker from pacing	None	None
DDD	Both	Both	Response can be both triggering and inhibitory	None	None

Set the mode according to the need and device

Step 5: Know the Complication and Management

Complications

- *Complications as with any route*—pericardial friction rub, arrhythmia, right ventricular perforation, cardiac tamponade, infection, arterial injury, diaphragmatic stimulation, phlebitis, and pneumothorax
- *Complications of internal jugular venous and subclavian access*—pneumothorax, carotid arterial injury, venous thrombosis, and pulmonary embolism
- *Complication of antecubital venous access*—dislodgement of the pacing electrode from a stable ventricular or atrial position (movement of the arm) and infection (more with this approach than others)
- *Complication of femoral access*—deep venous thrombosis and infection

Management

- Optimum knowledge about the anatomy and the procedure
- Ability to evaluate the correct placement and the desired rhythm
- Strict intra- and postprocedural asepsis.

Step 6: Troubleshooting

- *Satisfactory pacing not achieved*: Withdraw the wire into the right atrium and repeat the attempt to cross the tricuspid valve.
- *Difficulty in positioning the wire at the apex of the right ventricle*: Pass the tip of the wire into the right ventricular outflow tract and withdraw gently while rotating between the index finger and the thumb. When the tip is at a downward angle, advance toward the apex.
- *No spikes seen and no output*: Suspect failure of the battery or generator or a loose connection.
- *Spikes seen but no capture*: Suspect a loose connection but may be due to exit block causing a high threshold. Check the position of the pacing wire and consider repositioning.

Step 7: How to Monitor

Assess rhythm for appropriate pacemaker function:

- *Capture*: Is there a QRS complex for every ventricular pacing?
- *Rate*: Is the rate at or above the pacemaker rate if in the demand mode?
- *Sensing*: Does the sensitivity light indicate that every QRS complex is sensed?

Step 8: Postprocedural Investigations and Precautions

- A chest X-ray is needed to confirm a satisfactory position of the wire and to exclude a pneumothorax.
- Ensure the pacing wire is secured.
- Check and document all connections, battery, and control settings every 4 h and document.
- Sterile precaution is required as in handling a central line.
- Keep the pulse generator dry and the controls protected from mishandling.
- Protect the patient from electromicroshock and electromagnetic interference by covering the exposed wires and the pulse generator, wearing gloves when handling exposed wires; avoid any patient contact with electrical apparatus.

Suggested Reading

Cooper DH, Krainik AJ, Lubner SJ, Reno HEL. Washington manual of medical therapeutics. 32nd ed. Department of Medicine, Washington University School of Medicine. Published by Lippincott Williams & Wilkins; 2007. p. 150.

Ellenbogen KA, Wood MA. Cardiac pacing and ICDs. 5th ed. Malden: Blackwell Publishing; 2008.

Fink MP, Abraham E, Vincent JL, Kochanek PM. Textbook of critical care. 5th ed. Philadelphia: Elsevier Saunders; 2005. Chapter 211, p. 1817–24. *It gives a comprehensive description of the pacemaker and procedure of insertion and enlists the indications for temporary pacing.*

Irwin RS, Rippe JM. Irwin and Rippe's intensive care medicine. 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2008. Chapter 5, p. 66–72. *Detailed procedure and indication with pictorial depiction.*

Ryan TJ, Antman EM, Brooks NH, Califf RM, Hillis LD, et al. Update: ACC/AHA guidelines for the management of patients with acute myocardial infarction: executive summary and recommendations. Circulation. 1999;100:1016–30. *A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee on Management of Acute Myocardial Infarction).*

Percutaneous Tracheostomy

46

Rajesh Chawla, Sudha Kansal, and Munish Chauhan

Case Vignette

A 50-year-old male patient, a known case of chronic obstructive pulmonary disease with ischemic cardiomyopathy and renal failure, was admitted to the hospital with acute breathlessness. He was drowsy and unable to maintain oxygenation on noninvasive ventilation. He was put on invasive ventilation and he got better. A spontaneous breathing trial was tried several times, but he could not be weaned off the ventilator for 10 days. Percutaneous tracheostomy (PCT) was planned. During pre-procedure assessment, a pulsation was palpated over the area of incision raising the suspicion of a high-riding innominate artery.

PCT is a bedside procedure performed usually in an ICU setting. This uses the Seldinger technique and is associated with lesser postprocedure complications.

Step 1: Assess the Need for Tracheostomy and the Advantage of PCT

A. *Indications*

- Securing the airway
  - Temporary—to aid weaning after long-term mechanical ventilation
  - Permanent—airway protection in neurological patients

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- Tracheal toileting and airway protection
  - In the patient with excess or thick secretions who is not able to expectorate
  - Generalized weakness—neuromuscular disease or central cause
  - Altered mentation—unable to maintain airways
- Relief of nonemergent upper airway obstruction
  - Once initial airway stabilization has been done via trans laryngeal intubation/emergency cricothyroidotomy

B. *Advantages of PCT over surgical tracheostomy*

- Blunt dilatation causes less tissue trauma and devitalization than sharp dissection.
- It may lead to lower rates of hemorrhage, stomatitis, and cosmetic deformity.
- The tracheostomy tube is fitted tightly against the stoma.
- The interval between the decision and the actual procedure is shorter.
- It can be done at the bedside in the ICU, avoiding a potentially hazardous transfer of critically ill patients to the operating room.
- Savings in cost of operating room personnel and equipment can be achieved.

Step 2: Select Patient for PCT

- The patient should be hemodynamically stable as much as possible.
- FiO_2 should be below 0.6.
- Positive end-expiratory pressure should be less than 10 cm H_2O.
- History of uncomplicated translaryngeal intubation is obtained.
- Cricoid cartilage is palpable at least 3 cm above the sternal angle during appropriate neck extension.

Step 3: Check for the Contraindications

There are no absolute contraindications. Suggested contraindications are not supported by adequate data but are decided on merit depending on the operator experience and protocols of the center involved (Table 46.1).

Table 46.1 Contraindications to PCT

Inability to identify anatomical landmarks	Surgical skin site infection
Previous major neck surgery completely obscured the anatomy	Midline neck mass
Emergency airway control	High positive end-expiratory pressure (>10–20 cm H_2O)
Repeat tracheostomy	Severe coagulopathy
Age less than 15 years	Tracheomalacia
Cervical fixation/injury/fracture	Obese/thick neck

Step 4: Decide Timing

- The decision about tracheostomy requires anticipation of the duration of expected mechanical ventilation and the expected benefits and risks of the procedure.
- The decision of timing must be individualized depending upon the indication.
- Time of PCT could be 7–14 days of intubation though some professional bodies recommend as early as 5–7 days.
- It can be performed earlier (<7 days) for anticipated prolonged ventilation, for increased patient comfort and less sedation requirements. In some cases, it can increase the chances of earlier liberation from ventilator and discharge from ICU.

Step 5: Obtain Informed Consent

- Discuss the prognosis of the patient and the need for the procedure.
- Explain the advantages and disadvantages of the procedure and the available options in detail. Communicate with the patients or their surrogates.
- Explain the detailed procedure, the benefits, the risks, and the alternatives in the language they understand.
- Document the consent and get it signed.
- In case of emergency, when the patient is unconscious and the surrogates are not available, document the situation clearly and perform the procedure.
- Discuss end-of-life options and goals of care with the family and patient (if possible) before the procedure.

Step 6: Form Your Team

- The operating physicians.
- One physician, managing the upper airway and bronchoscope, manipulates the tube to allow PCT.
- The paramedical staff/technician who assists with the bronchoscope and handling of the endotracheal tube.
- Another paramedical staff monitoring the vitals and administering medication.

Step 7: Prepare for the Procedure

- A PCT set as per the type decided by the physician
- A bronchoscope and its attachments
- Continuous monitoring of ECG, blood pressure, and oximetry
- Functioning intravenous access
- A sterile setup with enough sterile linen and instruments for dissection and retraction
- A crash cart with a laryngoscope and endotracheal tubes and emergency drugs

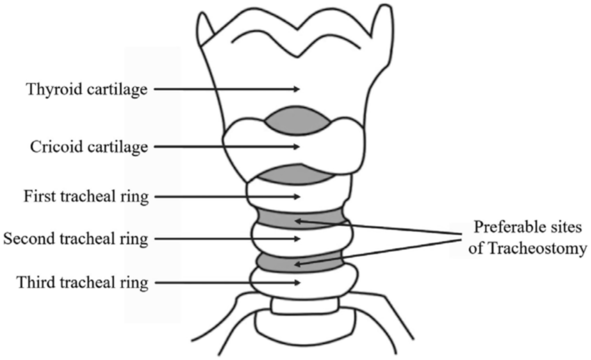


Fig. 46.1 Tracheal anatomy

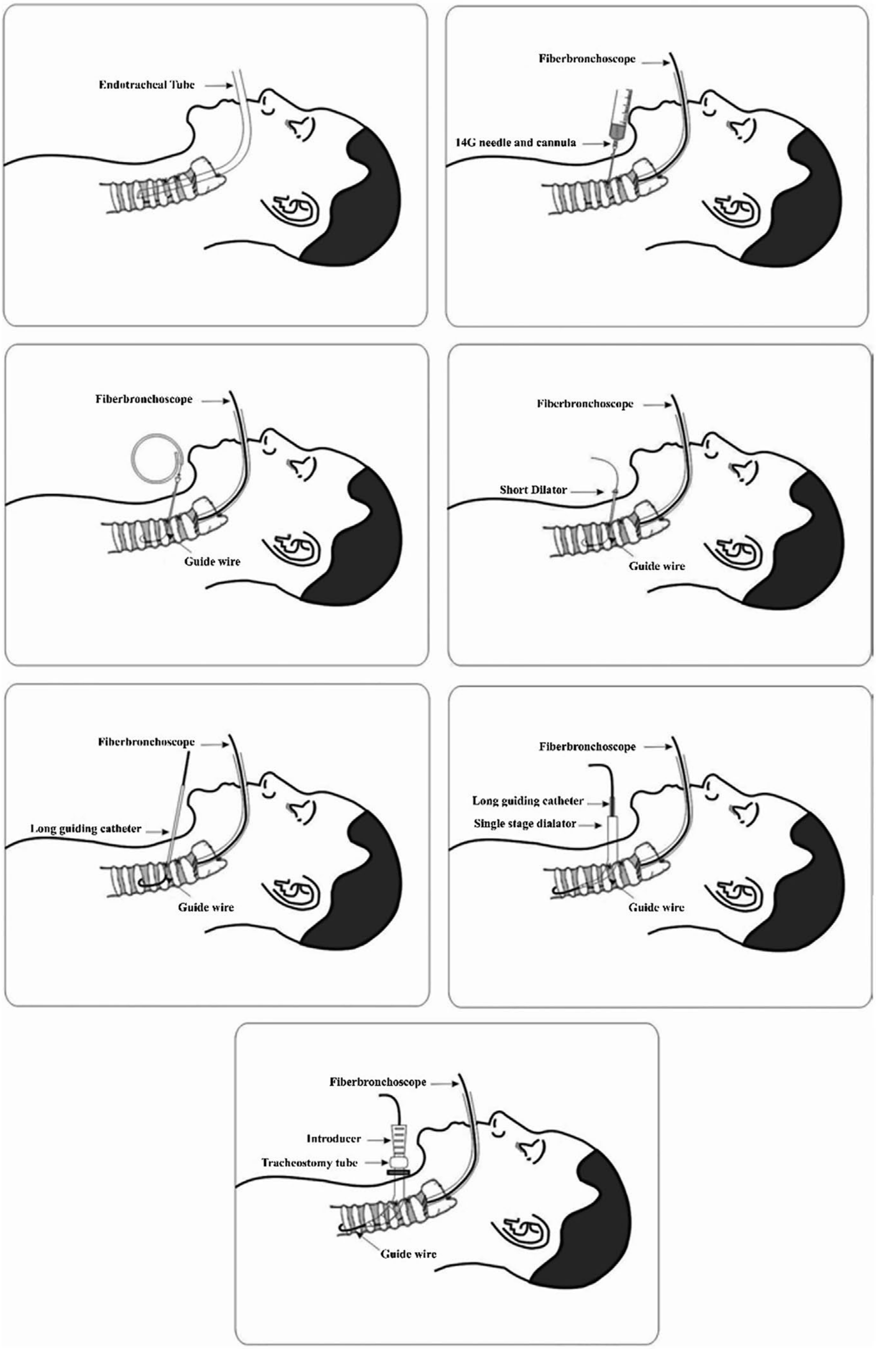
- Suction equipment
- Medications
  - 1% xylocaine with epinephrine
  - Sedating and paralyzing agents

Step 8: Identify Anatomy (Fig. 46.1)

- Tracheostomy is carried out at least one to two rings beyond the cricoid.
- The tracheostomy tube is entered between the second and third cartilage rings or between the third and fourth cartilage rings.
- In a too-high tracheostomy (close to cricoid), there is a risk of subglottic stenosis.
- In a too-low tracheotomy, there is a risk of bleeding from the brachiocephalic trunk.

Step 9: Perform Percutaneous Tracheostomy

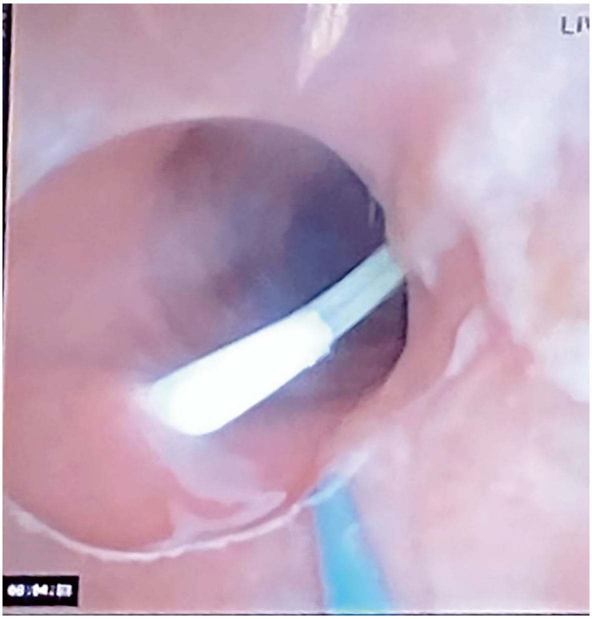
- *Ciaglia method (Blue Rhino PCT kit—Cook Critical Care Inc, Bloomington, IN and Portex® ULTRAperc® kit—Helmier)* (Figs. 46.2, 46.3, 46.4, 46.5, 46.6, 46.7, and 46.8). The operator should familiarize themselves with the components of the kit before proceeding.
  1. Continuously monitor vital signs, pulse oximetry, and complete ventilatory parameters.
  2. Take a time-out to verify patient identity and procedure to be performed.
  3. Ventilate with 100% oxygen during the procedure.
  4. Counsel and comfort the patient if he/she is conscious.
  5. Sedate and paralyze the patient before positioning.
  6. Extend the neck to open the tracheal interspaces, carefully supporting the vertex using a sandbag beneath the shoulders and the head ring.
  7. Prepare the surgical field with an alcohol-containing solution and drape it.
  8. Verify the anatomy and identify the neck structures and landmarks. A preprocedure ultrasound may be done if anatomy is not clear (e.g., morbid obesity).


Endotracheal Tube
Fiberbronchoscope
14G needle and cannula
Fiberbronchoscope
Guide wire
Fiberbronchoscope
Short Dilator
Guide wire
Fiberbronchoscope
Long guiding catheter
Guide wire
Fiberbronchoscope
Long guiding catheter
Single stage dialator
Guide wire
Fiberbronchoscope
Introducer
Tracheostomy tube
Guide wire

Figs. 46.2, 46.3, 46.4, 46.5, 46.6, 46.7, and 46.8 Ciaglia method

9. The local anesthetic with epinephrine is infiltrated into the surgical site.
10. Check all parts of the tracheostomy set. Check the tracheostomy balloon by inflating and collapsing it.
11. Make a transverse skin incision approximately 2 cm over the first and second tracheal interspace, approximately two fingers' breadth above the sternal notch.
12. Dissect the wound bluntly with a hemostat through the subcutaneous fascia.
13. Withdraw the endotracheal tube (ET) into a position above the first tracheal interspace under bronchoscopic guidance, after deflating the ET cuff, till the subglottic area is visible. Reinflate the cuff. A quick sweep of the airways with the bronchoscope can be done to look for any secretions causing plugging. Position of the tube can also be confirmed with the transillumination of the bronchoscope's light through the surgical field.
14. Insert a 14-gauge cannula over the needle through the skin incision between either the first and second or the second and third tracheal rings under bronchoscopic guidance to postwall puncture of tracheal wall, aspirating for air (Fig. 46.3). The bevel of the needle should face caudally to direct the guidewire correctly. Always stay in midline.
15. Care should be taken to not to damage the ET cuff as air leak might ensue. Depending on the clinical situation, a new ET tube might be inserted or tracheostomy secured.
16. Withdraw the needle leaving the cannula in place.
17. Advance a J-tipped guidewire through the cannula beyond the carina under vision (bronchoscopic view: Figs. 46.9 and 46.10) and withdraw the cannula (Fig. 46.4).
18. Dilate the opening using the small dilator (Fig. 46.5).

Fig. 46.9 Bronchoscopic view visualizing the J-tipped guide wire being advanced over the cannula



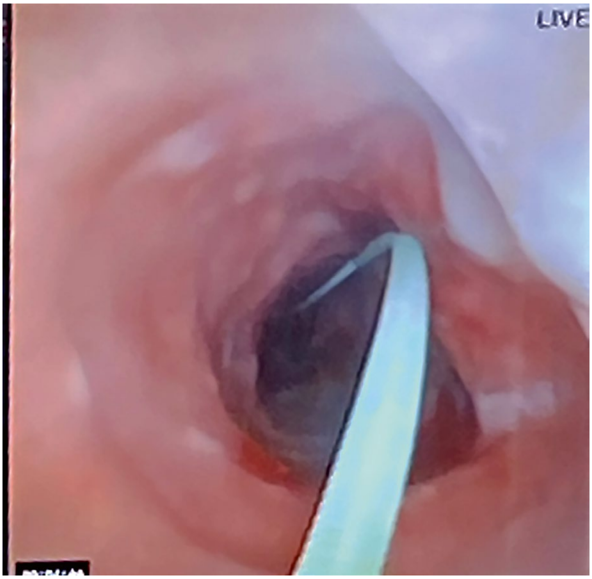


Fig. 46.10 Guide wire visualized in the trachea up until the carina

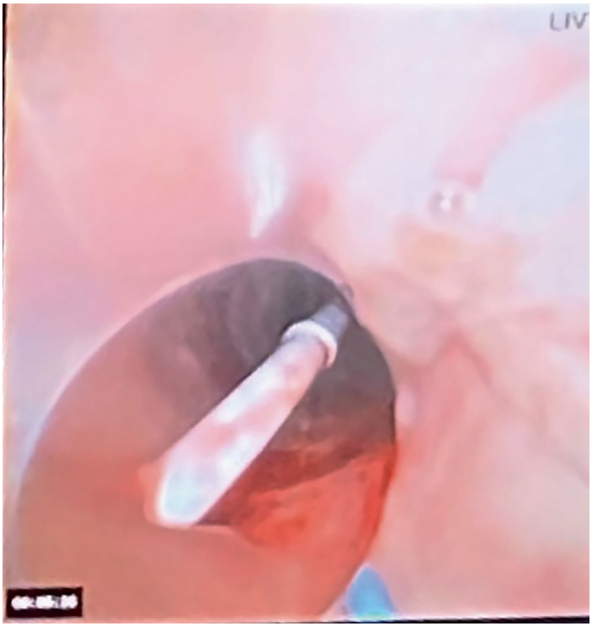


Fig. 46.11 Stiff protective sheath over the guidewire with "guard" visible

19. Insert a stiffer protective guiding catheter over the guidewire after withdrawing the cannula (Fig. 46.6) (bronchoscopic view Fig. 46.11).
20. Use a single, sharply tapered dilator with a hydrophilic coating and dipped in water-based jelly for complete dilatation in one step. The markings on the sides of the dilator indicate the depth to be inserted (Fig. 46.7). Always ensure control of the guidewire and the guiding catheter at all times to avoid migration into the trachea.

21. Withdraw the dilator leaving the guidewire and the stiff white guiding catheter assembly in place.
22. Once the tracheostoma has been dilated to the appropriate size, a tracheostomy tube is introduced into the trachea over the same guidewire using introducer dilators as an obturator (Fig. 46.8).
23. The guidewire assembly is removed leaving the tracheostomy tube in place.
24. Position is confirmed by bronchoscopic visualization with the neck flexed and/or end tidal carbon dioxide monitoring after resumption of ventilation through the tracheostomy tube.
25. The tube is sutured to the skin and also fixed with the provided thread around the neck. The oral ET tube is removed only after the tracheostomy tube is fixed safely. Apart from Cigalia method, other 2 techniques used commonaly are:
    - *Griggs guidewire dilating forceps*
        - Steps 1–15 as above.
        - The cannula is removed leaving the guidewire in place.
        - The Griggs guidewire dilating forceps are threaded over the guidewire into the soft tissue.
        - Open the forceps “dilating” the soft tissue and advance the forceps into the trachea.
        - The trachea is dilated to an aperture sufficient enough to accommodate the tracheotomy tube. The forceps is rotated by 90° and dilatation repeated.
        - An obturator is used to insert the tube over the guidewire.
        - The rest of the steps of fixation of the tube are same as above (Fig. 46.3).
    - *PercuTwist technique* (It contains a J-tipped guidewire, a scalpel, a large-bore introducer needle, the hydrophilically coated PercuTwist dilator, a specially designed 9.0-mm internal diameter PercuTwist tracheotomy cannula, and an insertion dilator.)
        - Steps 1–15 as above.
        - The PercuTwist single dilator is moistened to activate the hydrophilic coating.
        - Advance it over the guidewire into the soft tissue using a clockwise rotation.
        - Further rotation of the device engages the anterior tracheal wall and enlarges the aperture.
        - Once dilated adequately, the device is removed and replaced with the 9.0-mm tracheotomy tube fitted with the insertion dilator.

Ultrasound Guidance in Percutaneous Tracheostomy Instead of Bronchoscope

- Bedside ultrasonography is increasingly being used in ICU settings for various procedures and monitoring purposes. The aim is to decrease the risk profile of procedures and increase the success rate.

- In percutaneous tracheostomy, it is becoming increasingly beneficial in a select few scenarios like
  - Morbid obesity
  - Anatomical deformity: acquired or genetic
  - Thyromegaly
  - Overlying vascular structure
- Landmark identification can be difficult in such cases, increasing risk of trauma, malposition, or failure of procedure

Technique:

- Steps 1–7 as above
- Step 7: Use a 2D ultrasound using a linear array probe (probe should be covered with sterile camera cover)
  - Sagittal view (Fig. 46.12): Note the position and anatomical relation of all landmarks like the thyroid and cricoid cartilage, the tracheal rings, the thyroid gland, and the carotid and jugular vessels.
  - Transverse view (Figs. 46.13 and 46.14): Any aberrant vessels/structure encroaching the proposed surgical area should be noted. Can use color Doppler also. If needed, tracheostomy tube size can be decided.
- Steps 8–12 as above
- Step 13: Insert a 14-gauge cannula over the needle through the skin incision under real time imaging in the sagittal plane to guide the level of insertion in the midline. Then turn the probe by 90° for a transverse view to guide the needle tip (represented by an acoustic shadow) toward the midline. You might need to direct the probe bit caudally to keep track of the needle tip.
- The sagittal view can be difficult to attain in some cases like short necked patients. In them, we can use the transverse view for puncture.
- Rest of the steps as detailed above for different types of tracheostomy.

Modifications to the procedure in lieu of COVID-19 status:

- Complete paralysis with neuromuscular blocking agents:

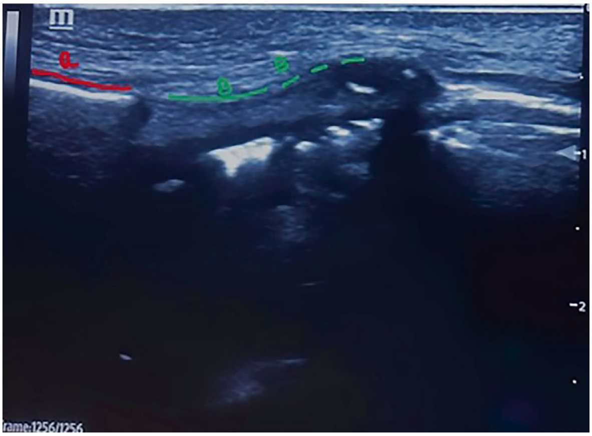


Fig. 46.12 Sagittal view: (**a**) cricoid and (**b**) tracheal rings

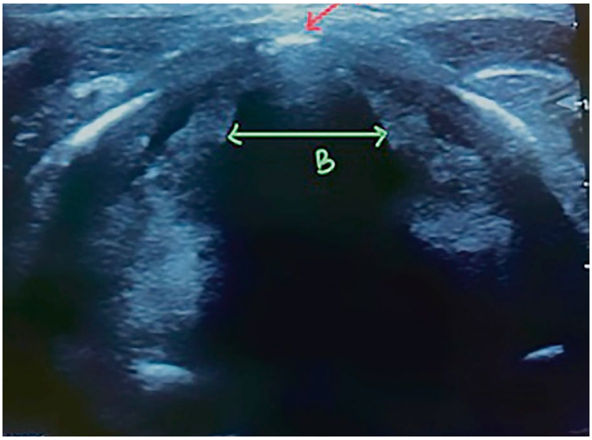


Fig. 46.13 Transverse view: (**a**) cricoid and (**b**) subglottic space

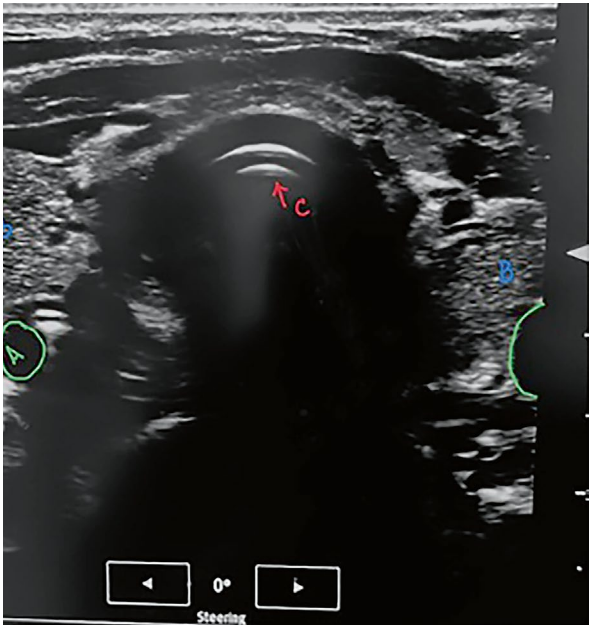


Fig. 46.14 Transverse view (lower level): (**a**) common carotid artery, (**b**) thyroid gland, and (**c**) tracheal rings

  - Abolition of cough reflex
  - Apnea during circuit disconnection
- Minimum number of trained personnel wearing PPE

Step 10: Postoperative Care of the Tracheostomy Tube

- Wound and dressing care
  - Daily examination of the stoma is needed to identify infections or excoriations of the skin.

  - Keep the wound clean and free of blood and secretions, especially in the immediate posttracheostomy period.
  - Dressing changes should be performed at least twice a day and when the dressings are soiled.
  - When changing dressings and tapes, special care is needed to avoid accidental dislodgement of the tracheostomy tube.
  - The inner cannula if used is changed daily or more frequently if necessary.
- Humidification
  - Humidification of inspired gases prevents obstruction of the tube by inspissated secretions and maintains mucociliary clearance and cough reflex.
  - Heat and moisture exchangers are preferred over heated humidifiers.
- Suctioning
  - Airways should be cleared of excess secretions to decrease the risk of lung infection and airway plugging.
  - Suctioning is frequently required in patients with poor or ineffective cough.
  - Suctioning should remove the maximal amount of secretions and cause the least amount of airway trauma. Thus, practice slow suctioning.
    1. Routine suctioning, however, is not recommended.
    2. Upper airway suctioning should also be done periodically to remove oral secretions and to minimize stasis of pooled secretions above the tracheotomy cuff with subsequent potential aspiration into the lower airways.
- Change tracheostomy tube
  - In case of a functional problem with the tube, such as an air leak.
  - If the lumen is narrowed due to the buildup of dried secretions.
  - Switching to a new type of tube.
  - May downsize the tube before decannulation.
  - Do not change the outer cannula, unless the cuff is damaged, in the initial 5–7 days as the tract is not stable.
- Tube cuff pressure
  - Tracheotomy tube cuffs require monitoring to maintain pressures in a range of 20–25 mmHg.
  - Cuff pressures should be monitored with calibrated devices.
  - Record at least once every nursing shift and after manipulation of the tracheotomy tubes.
  - Maintain the tube in a central position, avoiding angling and contact between tracheal mucosa and the tube to avoid damage by the distal end.
  - Avoid traction as well as unnecessary movement of the tube.
- Nutrition
  - Feeding may become complicated because of tube interference with normal swallowing and airway control.
  - It decreases laryngeal elevation during swallowing and an inflated cuff may compress the esophagus. So, it may deflate a little.
  - Keep the head end elevated to 45° during periods of tube feeding.
  - Before attempting oral feedings, several objective criteria must be met.

- The patient must be consistently alert and able to follow complex commands.
- Adequate cough and swallowing reflexes.
- Adequate oral motor strength.
- A significant respiratory reserve.
- Assess swallowing function.
- Oral feeding is done under supervision of a caregiver and carefully assessed for aspiration or regurgitation.

Step 11: Manage Complications

- Early complications (until 7 days)
  1. Tube displacement
     - Management—endotracheal intubation to establish airway. Replace the tracheostomy tube under less urgent conditions, always under fiber-optic guidance as there is a danger of entering a false tract. If it fails, intubate orally.
     - Prevention—proper placement of the stoma, avoid excessive neck hyperextension and/or tracheal traction, apply sufficiently tight tracheostomy tube retention tapes, and suture tracheostomy tube flange to the skin.
     - Displacements after 7 days are managed by simply replacing the tube as the tract is well formed.
  2. Tube obstruction
     - By mucus, blood clots, displacement into surrounding soft tissues, or abutment of the tube's open tip against the tracheal wall.
     - Reposition or suction thoroughly; deflate cuff as a temporizing measure.
     - If it fails, replace the tube immediately or intubate orally.
  3. Pneumothorax/pneumomediastinum
     - Pleura can be damaged during tracheostomy.
     - The incidence of pneumothorax after tracheostomy ranges from 0% to 5%.
     - Many surgeons routinely obtain a postoperative chest radiograph though optional.
     - Immediate tube thoracostomy.
  4. Subcutaneous emphysema
     - Positive-pressure ventilation or coughing against a tightly sutured or packed wound causes this.
     - It can be prevented by not suturing the wound around the tube.
     - It resolves spontaneously within a few days.
     - A chest radiograph should be done to rule out a pneumothorax.
  5. Hemorrhage
     - Usually, minor postoperative venous ooze is the most common complication.

  - Elevate the head of the bed, pack the wound, and/or use homeostatic materials.
  - Major bleeding can occur in up to 5% of tracheotomies.
  - Hemorrhage from the isthmus of the thyroid gland.
  - Injury to the transverse jugular vein.
  - May require an exploration.
6. Stomal infections
   - Good stoma care
   - Early use of antibiotics but do not use prophylactic antibiotics
7. Others
   - Arrhythmia
   - Hypotension
   - Hypoxia/hypercapnia
   - Loss of airway control
   - Bacteremia
   - Esophageal injury
   - Cardiorespiratory arrest
   - Tracheolaryngeal injury

- Late complications (>7 days)
  1. Tracheoinnominate artery fistula (<0.7% cases)
     - Occurs due to erosion through the trachea into the artery due to excessive cuff pressure or by angulation of the tube tip against the anterior trachea
     - Risk increased by the following:
       - Low placement of tracheotomy
       - High-pressure cuffs
       - Excessive head or tracheostomy tube movement
       - Malnourishment
     - Management
       - Evaluate even minor bleeds
       - Hyperinflation of the cuff; lower neck incision with blind digital compression on the artery may be attempted in a resuscitative effort
       - Operative intervention
  2. Dysphagia and aspiration
     - Due to causes discussed under “nutrition”
  3. Tracheal stenosis
     - Approximately 1–2% cases
     - Caused by
       - Ischemia
       - Devascularization
       - Chemical erosion
       - Infection
     - Due to high-pressure cuffs
     - Forced angulation of a stiff tube
     - Hyperinflation of the cuff that results in tracheal damage

- Site of stenosis may occur at the:
  - Stoma
  - Cuff
  - Tip of the tracheotomy tube

4. Tracheoesophageal fistula
   - Less than 1% of patients
   - Mostly iatrogenic during procedure
   - Erosion by the tracheotomy cuff
   - Tube angulation with pressure against the posterior tracheal wall
   - More common with a nasogastric tube in place as well
   - Suspect if:
     - Cuff leaks
     - Abdominal distention
     - Recurrent aspiration pneumonia
     - Reflux of gastric fluids through the tracheostomy site
   - Diagnosed by endoscopy or contrast studies
   - Requires surgery or esophageal and tracheal stent
5. Granuloma formation
   - A foreign body reaction to the tracheotomy tube or part.
   - Treated with the YAG laser.
   - Granulomas at the lower end of the tracheotomy tube require bronchoscopic removal, providing temporary relief.
6. Persistent tracheocutaneous stoma
   - Can occur when tube has been left in position for a prolonged period.
   - Surgical closure is required.
7. Tracheomalacia
   - Weakening of the tracheal wall
     - Ischemic injury to the trachea
     - Followed by chondritis
     - Then destruction and necrosis of the tracheal cartilage
   - Collapse of the affected portion of the trachea with expiration
     - Airflow limitation
     - Air trapping
     - Retention of airway secretions
   - Cause of weaning failure from mechanical ventilation.
   - A short-term therapeutic approach to tracheomalacia is to place a longer tracheostomy tube to bypass the area of malacia.
   - Long-term treatment options include stenting, tracheal resection, or tracheoplasty.

Step 12: Decannulation

1. Criteria
   - Stable arterial blood gases
   - Absence of distress

- Hemodynamic stability
- Absence of fever or active infection
- $PaCO_2 < 60$ mmHg
- Absence of delirium or psychiatric disorder
- Normal endoscopic examination or revealing stenotic lesion occupying less than 30% of the airway
- Adequate swallowing
- Able to expectorate

2. Procedure
    - The deflated-cuff tracheotomy occlusion procedure
        - Occlude the opening of the tube with the cuff deflated by a gloved finger observing the patient for objective signs of respiratory distress.
        - In case of problems, promptly return the patient to breathing through the tracheotomy tube and perform a fiberendoscopic examination to check for upper airway obstruction.
        - If no lesions are present, consider whether the tube is not too large and try again after changing the tube.
        - The tube can be removed, and the opening is covered with sterile dressings. The wound spontaneously heals in 10 days in most cases.
    - Use tracheotomy button or speech valve in patients with prolonged tracheotomy.

Suggested Reading

Al-Ansari MA, Hijazi MH. Clinical review: percutaneous dilatational tracheostomy. Crit Care. 2006;10:202. *This review discusses the general issues related to PCT and the evidence-based recommendations, using the best available evidence, relating to various issues.*

Angel LF, Simpson CB. Comparison of surgical and percutaneous dilational tracheostomy. Clin Chest Med. 2003;24:423–9. *This review includes previous data relating to comparison of open tracheostomy to open procedure, the safety profile, and other benefits of one over the other.*

De Leyn P, Bedert L, Delcroix M, Depuydt P, et al. Tracheotomy: clinical review and guidelines. Eur J Cardiothorac Surg. 2007;32:412–21. *Guidelines are developed by the Belgian Society of Pneumology and the Belgian Association for Cardiothoracic Surgery on tracheotomy for mechanical ventilation in adults.*

deBoisblanc BP. Percutaneous dilational tracheostomy techniques. Clin Chest Med. 2003;24:399–407. *This study discusses the various types of techniques developed over the years and their pros and cons and their comparison to the open procedure.*

Ernst A, Critchlow J. Percutaneous tracheostomy—special considerations. Clin Chest Med. 2003;24:409–12. *A part of the review series in the journal that describes the efficacy of the procedure in special conditions considered to be contraindications to PCT.*

Hashimoto DA, et al. Percutaneous tracheostomy. N Engl J Med. 2020;383:e112. *A review article.*

Heffner JE. Tracheostomy application and timing. Clin Chest Med. 2003;24:389. *This review discusses the indications of tracheostomy and various types of the procedure along with the advantages and disadvantages of one over the other.*

Rudas M. The role of ultrasound in percutaneous dilatational tracheostomy. AJUM. 2012;15(4):143. *Ultrasound is a good guide for percutaneous dilatational tracheostomy.*

Post-tracheostomy Care in ICU Patients

47

Rajesh Chandra Mishra, Ruchira Khasne,
and Meera Pandey

Case Vignette

A 50-year-old male with motor neuron disease, who has had a cuffed tracheostomy for 2 months and is on home ventilation, was admitted with respiratory distress. On admission, he has labored breathing, low oxygen saturation, and diminished air entry in his right lung. It was difficult to negotiate a suction catheter. An emergent change of the tracheostomy tube was done with relief of dyspnea.

Caring for a tracheostomy patient in ICU is a challenging task. Tracheostomy is lifesaving in patients with upper airway obstruction, helps in weaning in difficult-to-wean patients, and facilitates secretion removal and early mobilization. In comparison to endotracheal intubation, tracheostomy reduces dead space, facilitates vocalization, and improves pharyngeal muscle strength. All these benefits can only be ensured if the tracheal tube is patent, properly placed in midline, and free of complications. If appropriate care is not taken, tracheostomy tube itself can be fatal. The patency of the tracheostomy tube is ascertained by nontraumatic suction protocol as and when required. Midline

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placement of the tube should be ensured by appropriate suturing or perfectly fitting tie, also known as tracheostomy collar. Ventilator circuit weight and patient movement can contribute to tube dislodgement, displacement, life-threatening bleeding, and in long-term trachea-esophageal fistula. Excessive cuff pressure for a longer duration can cause tracheal stenosis or tracheomalacia. The very purpose of having a well-placed multidisciplinary tracheostomy team is to provide optimum, complication-free care to get maximum benefit and avoid further harm.

Step 1: Initiate Tracheostomy Care Immediately After Insertion

- Tracheostomy tube insertion can be done either by percutaneous method or surgical tracheostomy procedure.
- Confirm tube placement by auscultation and monitoring SpO_2, $EtCO_2$, peak pressures, and hemodynamics.
- Confirm the position of the tube by chest X-ray where the distal end of the tracheostomy tube should be 4–6 cm above the carina. USG of the airway is a point-of-care test for confirming the position of the tracheostomy tube in situ.
- Secure the tube properly; tube tie or collar should not be very tight or very loose (movement limited to 1 finger width).

Step 2: Evaluate for Bleeding

- Bleeding can be primary in the immediate post-op period or can be secondary bleeding in the intermediate period.
- Bleeding can be at the stoma site or in the trachea. A small amount of bleeding is expected and is often self-limiting. However, continuous or profuse bleeding requires surgical reexploration and/or vessel ligation. Besides that, anterior tracheal injury, posterior tracheal perforation, and injury to paratracheal structures can lead to bleeding.

Step 3: Evaluate for Aspiration

- The tracheostomy cuff should be kept inflated for effective ventilation and further prevention of aspiration.
- Cuff pressure should be frequently monitored and maintained between 20 and 25 cm of water. Higher cuff pressure can cause long-term complications such as tracheomalacia, tracheoinnominate artery fistula, tracheal ulcerations, fibrosis, stenosis, and tracheoesophageal fistula, whereas lower cuff pressure can lead to

leakage of secretions around the cuff and subsequent ventilator-associated pneumonia (VAP).

- Caution should be used while measuring cuff pressure as it may entail transient deflating of the cuff, which may lead to aspiration.
- Persistent cuff leaks should be promptly recognized and treated. It can be because of malfunctioning of the pilot balloon and the trachea must have lost its rigidity owing to tracheomalacia. Tracheomalacia is diagnosed with the help of a CT scan of the airway and bronchoscopy. However, if tracheomalacia is diagnosed, the patient may need a long flange tracheostomy tube to bypass the damaged part and avoid further damage and tracheal collapse.

Step 4: Evaluate for Displacement and Decannulation

Accidental displacement and decannulation can occur at any time and can be life-threatening.

- The term dislodgement means when the tube is partially displaced and the tip lies within a false passage anterior to the trachea.
- The term decannulation means when the tube is completely withdrawn from the stoma.
- Replacement tracheostomy tube set should be always kept bedside.
- This complication is commonly observed when the tie is loose, edema around the neck, excessive coughing, agitation, undersedation, morbid obesity, short tracheostomy tube, technical difficulties while placing the tube, and traction caused by the weight of the ventilator circuit.
- Replacement of the tube is easier if the stoma is matured. With an immature stoma (less than 1 week old), tissue planes are likely to collapse, which makes replacement of tube difficult.
- Attempt to blindly insert and ventilate may cause formation of false passage, leading to subcutaneous emphysema and pneumothorax.
- In case of complete decannulation, immediate intervention is to maintain oxygenation by bag and mask and if required orotracheal intubation if replacement of tube is difficult.
- Replacement of the tube should be with an obturator in place, which facilitates tube placement by acting like a stylet.

Step 5: Evaluate for Tube Blockage (Fig. 47.1)

- Suspect tube block, if the patient is in respiratory distress or having stridor, desaturating, using accessory muscles of respiration and manual resuscitator bag, has offered some resistance.
- In a patient on a ventilator, one can find a serial drop in tidal volume or increase in peak pressure to diagnose tube blockage.

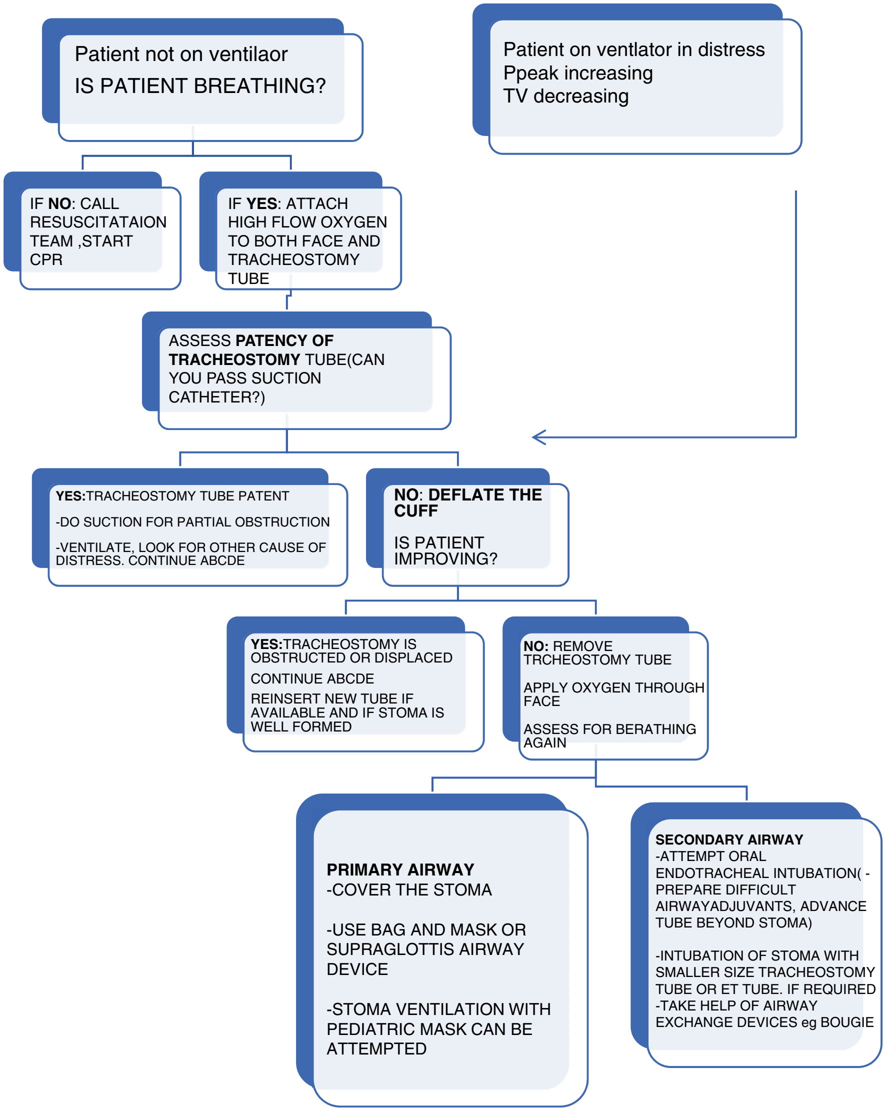

Patient not on ventilaor
IS PATIENT BREATHING?
Patient on ventlator in distress
Ppeak increasing
TV decreasing
IF NO: CALL RESUSCITATAION TEAM ,START CPR
IF YES: ATTACH HIGH FLOW OXYGEN TO BOTH FACE AND TRACHEOSTOMY TUBE
ASSESS PATENCY OF TRACHEOSTOMY TUBE(CAN YOU PASS SUCTION CATHETER?)
YES:TRACHEOSTOMY TUBE PATENT
-DO SUCTION FOR PARTIAL OBSTRUCTION
-VENTILATE, LOOK FOR OTHER CAUSE OF DISTRESS. CONTINUE ABCDE
NO: DEFLATE THE CUFF
IS PATIENT IMPROVING?
YES:TRACHEOSTOMY IS OBSTRUCTED OR DISPLACED
CONTINUE ABCDE
REINSERT NEW TUBE IF AVAILABLE AND IF STOMA IS WELL FORMED
NO: REMOVE TRCHEOSTOMY TUBE
APPLY OXYGEN THROUGH FACE
ASSESS FOR BERATHING AGAIN
PRIMARY AIRWAY
-COVER THE STOMA
-USE BAG AND MASK OR SUPRAGLOTTIS AIRWAY DEVICE
-STOMA VENTILATION WITH PEDIATRIC MASK CAN BE ATTEMPTED
SECONDARY AIRWAY
-ATTEMPT ORAL ENDOTRACHEAL INTUBATION(-PREPARE DIFFICULT AIRWAYADJUVANTS, ADVANCE TUBE BEYOND STOMA)
-INTUBATION OF STOMA WITH SMALLER SIZE TRACHEOSTOMY TUBE OR ET TUBE. IF REQUIRED
-TAKE HELP OF AIRWAY EXCHANGE DEVICES eg BOUGIE

Fig. 47.1 Evaluation for tube blockage

- Immediate suctioning will help to remove mucus and clear the partial block. It can be done either by close suction or open suction method and should be either at a defined frequency or on request.
- All aseptic precautions and strict hand hygiene protocols should be practiced at all times.
- However, if repeated suctioning or even manual ventilation fails to clear the block, then immediate replacement of the tube should be done.

- In case of difficult replacement, secure the airway and if required revision of the tracheostomy site is warranted.

Important Steps of Suctioning

Suctioning can be done by one or two persons.

- Step a: Each bedside should be equipped with a functional suctioning system, appropriate-size suction catheters, an oxygen source, a manual resuscitation bag, and a complete tracheostomy kit.
- Step b: Before suctioning, administer 100% oxygen. Choose an appropriate size suction catheter and apply the correct suction pressure of up to 10.6–20 kPa (80–150 mmHg). Ensure it is not greater than 20 kPa.
- Step c: With non-touch technique, suction catheter tip should be introduced at premeasured depth. The tip of the suction catheter remains within the tracheostomy tube and not beyond that while suctioning.
- Step d: Apply suction only while withdrawing the suction catheter by occluding the suction tubing with a gloved thumb to minimize tracheal injury.
- Step e: Ensure suctioning timing should not be more than 10 s and a maximum 3 passes of suction catheter at each time.
- Step f: The instillation of normal saline, to facilitate sputum clearance, is not a recommended practice, and it may actually be harmful.
- Step g: Suctioning should be discontinued if patient desaturates or arrhythmias occur.

Step 6: Take Care of Tracheostomy in the Intermediate Period

- During this period, patient should be monitored for stoma infection, tube block, skin breakdown, and secondary bleeding.
- Identify stoma infection by features of peristomal bleeding, signs of inflammation, infection, maceration, and granuloma formation.
- Stoma should be cleaned with cotton-tipped swabs soaked in normal saline at least once a day.
- Dressings should be done with sterile gauze, which should be placed below flanges. Gauze should not be cut as edges will fray and are potential sources of infection. Avoid using loose fibers around stoma as they can cause irritation.
- Ensure stoma and surrounding skin is thoroughly dried after cleaning. Secretions collected above the cuff may ooze out of the stoma site and cause wetness leading to skin maceration, excoriation, and infection at the stoma opening as well as at the tracheal opening.
- It is not recommended to use any cream or ointment or powder at stoma site.
- Consider subglottic suctioning as it can reduce incidence of late onset VAP.

Step 7: Ensure Humidification

- In patients with tracheostomy, the natural functions of warming, filtering, and humidifying the airway are lost, which makes secretions thick and prone to cause tube block. This in turn increases the risk of infection, impaired secretion removal, and microatelectasis. Thus, humidification is a very important aspect of tracheostomy care.
- Humidification techniques are active humidifier (presence of external sources of heat and water) and passive humidifier (utilization of patient's own temperature and hydration to achieve humidification in successive breaths). Passive humidifiers such as heat moister exchanger (HME) filters are also known as artificial noses (Fig. 47.2). It contains a condenser element, which retains moisture from every exhaled breath and returns it back to the next inspired breath and is more physiological.
- Thermovent is a type of passive humidifier that is a single-use heat and moisture exchanger designed for tracheostomy tubes. It comes with 15 mm connector to fit with all tracheostomy tubes. It provides effective humidification for spontaneously breathing patients whose upper airways are bypassed by a tracheostomy tube (Fig. 47.3).
- Following are the advantages of thermovent:
  - Reduces heat loss through the bronchopulmonary tree
  - Clear construction helps visual examination for secretions and obstruction
  - Facilitates suctioning and hence removal of secretions
  - Preserves humidity and minimizes damage to tracheal epithelial cells
  - Integrated port for oxygen helps provide extra oxygen if needed
  - Smooth rounded edges aid patient comfort.

According to the American Association of Respiratory Care (AARC) Clinical Practice Guidelines 2012, following are the contraindications:

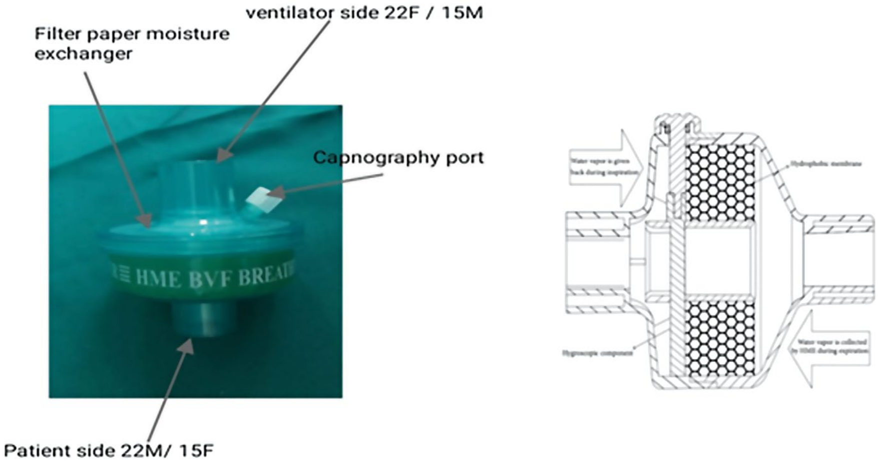

ventilator side 22F / 15M
Filter paper moisture exchanger
Capnography port
HME BVF BREAT
Patient side 22M/ 15F
Water vapor is given back during inspiration
Hydrophobic membrane
Hygroscopic component
Water vapor is collected by HME during expiration

Fig. 47.2 HME filter

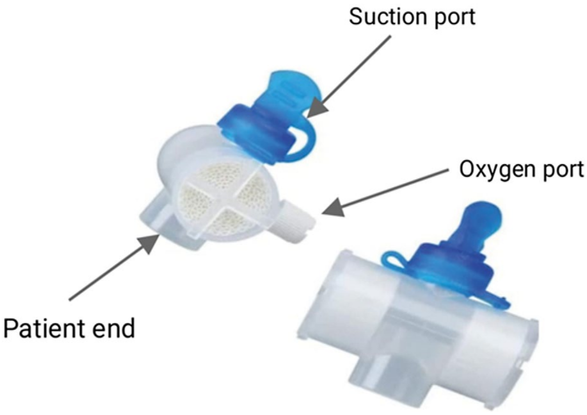

Suction port
Oxygen port
Patient end

Fig. 47.3 Thermovent

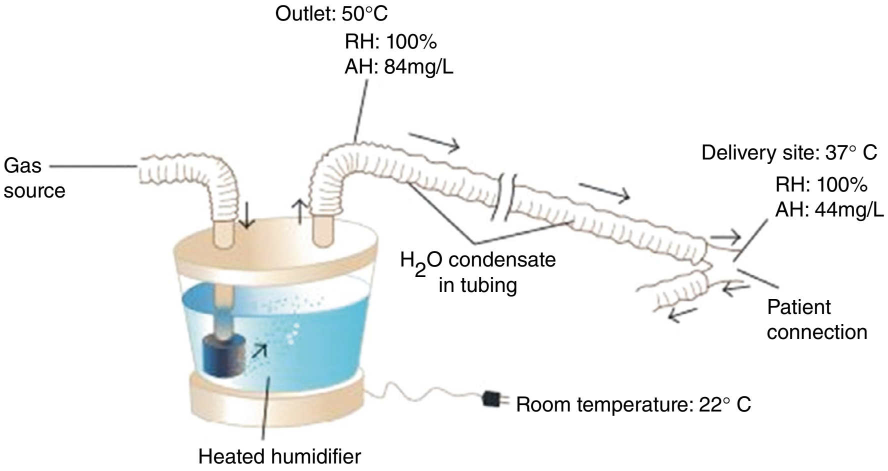

Outlet: 50°C
RH: 100%
AH: 84mg/L
Gas source
Delivery site: 37° C
RH: 100%
AH: 44mg/L
H2O condensate in tubing
Patient connection
Room temperature: 22° C
Heated humidifier

Fig. 47.4 Heated humidifier system

Contraindications for heat and moisture exchangers

- Patients with thick or copious secretions.
- Patients with limited respiratory reserve.
- In patients managed with low tidal volumes
- Difficult to wean patients
- Presence of endotracheal tube cuff leak
- Hypothermia (body temperature < 32 °C)

Active humidification: Following are the types of active humidifier (Fig. 47.4).

Heated humidifier system

Bubble humidifier: Gas is forced down a tube into the bottom of a container.

Passover humidifier: Gas passes over a heated water reservoir carrying water vapor to the patient.

1. *Counter flow humidifier*: Water is heated outside the vaporizer and then pumped into the humidifier. Gas flows in counter direction and is warmed to body temperature.
2. *Inline vaporizer*: Small plastic capsule is used in inline vaporizer to inject water vapor in inspiratory part of ventilator circuit. There is a small disk heater in the capsule for heating gas.

Different types of humidification heating devices are as follows:

1. Hot plate element: It sits at the bottom of the humidifier, the most commonly used humidifier.
2. Wrap around element: It surrounds the humidifier chamber.
3. Collar element: It sits between the reservoir and the outlet.
4. Immersion heater: It is placed directly inside the water reservoir.
5. Heated wire: It is placed in the inspiratory limb of the ventilator.

Advantages and Disadvantages of Each Humidification Method (Tables 47.1 and 47.2)

Table 47.1 Advantages of humidification method

Active humidifier	Passive humidifier
More reliability	Cost effective
Temperature monitoring present	Portable
Wide range of temperatures and humidity	User friendly
Alarms present	Helps to remove condensation
Reaches the maximum absolute humidity	No active efforts for working

Table 47.2 Disadvantages of humidification method

Active humidifier	Passive humidifier
Higher cost	Chances of occlusion
No filter	Increased dead space, work of breathing, PCO_2 levels
Condensation present	Increased resistance
Possibility of electrical shock and burns	Risk of rebreathing
Risk of contamination	Does not maintain temperature

Step 8: Identify and Avoid Skin Breakdown

- Stoma skin should be daily inspected and skin breakdown can be prevented with appropriate dressings.
- Sometimes suture precludes proper skin care till the stoma gets matured.
- Dressing with gauze is sufficient if secretions are minimum to moderate; however, if secretions are copious then its preferable to use polyurethane foam or hydrocolloid dressings.

- Foam dressing acts as an absorptive, moisture-retentive, and insulating, keeping the area dry while allowing oxygen to reach the area. If there is evidence of stoma infections, then dressings with ionic silver or nylon-impregnated silver dressings can be used.
- Ensure the tube is in a neutral position without any traction on the tube, particularly due to the oxygen delivery device that aggravates skin breakdown, tube dislodgement, and inadvertent decannulation.

Step 9: Identify Secondary Bleeding from the Stoma

- Frequent deep suctioning may lead to blood-tinged secretions. One has to be careful as undersuctioning can cause accumulation of secretions, mucus plug formation, and tube blockage.
- Tracheoinnominate fistula is rare but the deadly complication where the innominate artery is eroded through the trachea due to pressure necrosis from the tracheostomy tube cuff. It is associated with massive hemorrhage and the patient is exsanguinated within minutes. It occurs mostly in 3–4 weeks after the procedure.
- Management includes maintaining oxygenation, and cuff over inflation to cause the tamponade effect. Definitive options such as surgical repair or endovascular embolization can be considered.

Step 10: Consider Weaning and Decannulation of Tracheostomy

Prior to decannulation following should be ensured:

- Underlying pathology is resolved
- Underlying airway is patent
- Respiratory support is no longer required
- Patient has an effective cough
- Patient is able to swallow secretions
- Patient is sufficiently alert and stress free
- Patient is cardiovascular stable

Techniques of weaning and troubleshooting:

- Cuff deflation—in the absence of aspiration, continue for 24 h
- Gloved finger occlusion—observe for stridor
- Connect one-way speaking valve
- Decannulation cap
- Look for complications (Table 47.3)
- While usually uncomplicated, decannulation should be undertaken by experienced staff with equipment for immediate recannulation nearby.

Table 47.3 Probable complications following weaning

Problem	Cause	Solution
Respiratory distress	Poor airflow past tracheostomy either due to too large size tube, tracheal stenosis, oedema, or granulation tissue causing airway obstruction Patient underlying condition not improved	Consider for change to a smaller size +/− fenestrated tube Refer to ENT for upper airway evaluation If required fiberoptic bronchoscope evaluation
Excessive coughing	Secretion Anxiety Aspiration	Effective suctioning Reassure and explain procedure to patient Take help of therapist to improve deglutination

- Emergency intubation equipment and a trained airway expert should be immediately available if required.
- Nasogastric feeding should be stopped 4 h before decannulation and the gastric contents aspirated.
- Following decannulation, the stoma site should be dressed and allowed to heal by itself. The patient should be observed for 24 h before discharge to a ward.
- Stoma patency after decannulation is short lasting in percutaneous tracheostomy than in surgical tracheostomy

Long-Term Care of the Patient with Tracheostomy

Step 1: Select the Proper Tracheostomy Tube

- Polyvinyl chloride (PVC) and silicon tracheostomy tubes can be used.
- Single cannula tube is a low-pressure design available, which provides leak protection and aspiration prevention and allows positive pressure ventilation.
- Self-inflating cuff minimizes the potential for accidental overinflation and accidental decannulation.
- Silicone tubes are reusable, cost-effective, withstand repeated sanitization, and are tissue-friendly (Fig. 47.5).
- Dual cannula tubes are safer for long-term care in view of easy inner cannula removal for cleaning and in the event of tube obstruction. They help in weaning as the inner tube may increase the work of breathing (Fig. 47.6).
- Fenestrated tubes are also available (Fig. 47.7) with a single and double cannula, which facilitates speech and reduces the work of breathing in weaning. Not suited for positive pressure ventilation and with unhealthy tracheostomy wounds in view of the risk of surgical emphysema.
- Uncuffed tubes are used for patients who can protect their own airways, have an adequate cough reflex, and most importantly can manage their secretions. They remove the risk of tracheal damage caused by inflation of the cuff, may aid swallowing and communication.

- Adjustable flange and long-length tubes for particularly large neck patients due to obesity, goiter, or patients with tracheomalacia.
- Use of Olympic Trach button with adjustable depth may be used to keep the stoma patent after decannulation.
- This helps in the reintroduction of the tracheostomy tube if needed.

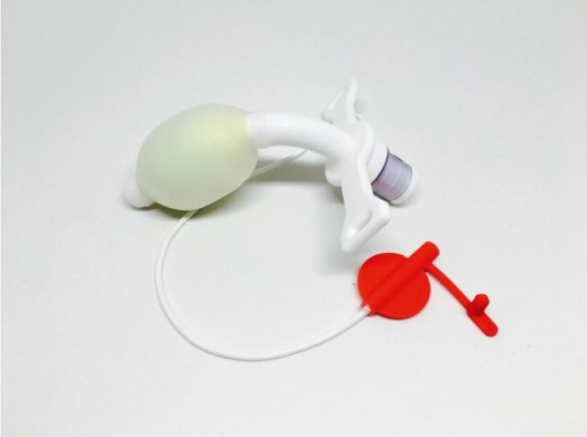


Fig. 47.5 Bivona silicone tubes

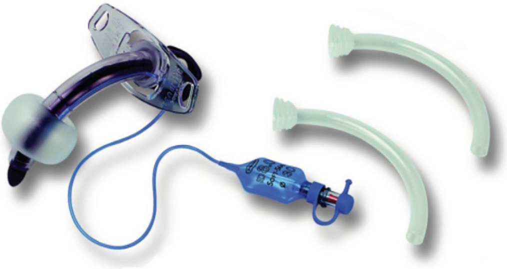


Fig. 47.6 Portex blue line ultra-tube

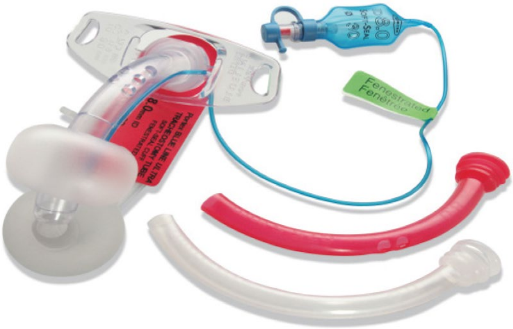


Fig. 47.7 Portex fenestrated tubes: red, inner cannula with fenestration; white, simple tube

Step 2: Stoma Care and Tube Change

- The inner cannula is regularly inspected at least twice daily to prevent narrowing or blockage but this may be required more or less frequently depending upon the quantity and tenacity of the patient's secretions.
- Decontamination from respiratory tract infection by cleansing the inner cannula with mild detergent is as effective as cleansing using an alcoholic chlorhexidine solution in reducing colony counts as per studies.
- Daily inspection of the oral cavity is mandatory. Stoma should be cleaned with saline and in case of infection with an antibacterial solution after sending a culture specimen.
- Chlorhexidine-based oral care is discouraged as it may lead to aspiration chemical pneumonitis.
- Small granulation tissue can be removed with silver nitrate and large may require surgical excision. Patients and relatives should be trained for stoma care and dressings.

Step 3: Provide Long-Term Proper Humidification

- In addition to adequate hydration and humidified gas supplies, patient may need an HME device as in acute care setting.
- Environmental temperature, as well as humidity, is an important concern in chronic care.
- Tracheal filter is a good option for passive humidification.
- A "tracheostomy mask" or collar can used for oxygenation, active humidification, and nebulization (Fig. 47.8).

Step 4: Perform Safe Suctioning

- Suctioning into the tracheostomy tube should not be done as a routine procedure.
- The patient must be assessed for signs of sputum in the airways. Where the patient can cough secretions independently into the top of the tracheostomy tube, these secretions can be removed with a clean Yankauer suction or tissue paper.

Step 5: Facilitate Speech and Communication

- The purpose of communication for critically ill patients is to help them maintain their identity as well as psychological, structural, personal, and social integrity.
- Nonverbal communication methods to be considered
  - Lip reading
  - Facial expression, coded eye blinking, and hand gestures

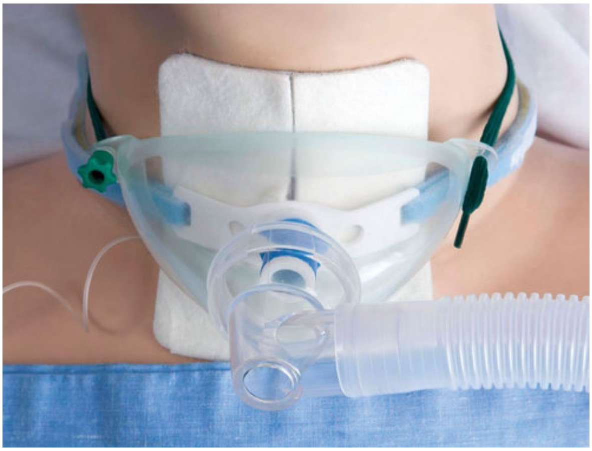
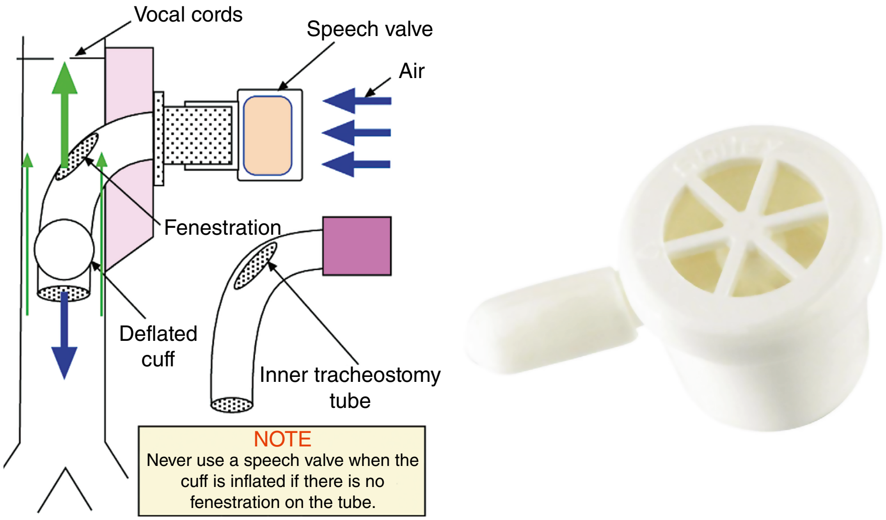


Fig. 47.8 Tracheostomy mask

  - Alphabet Board, Picture Board, and Phrase Books
  - Electronic Larynx and Electronic Communication Aids
- Verbal communication requires specially designed double lumen fenestrated tracheostomy tube and speaking valve (Fig. 47.9).

Steps for speaking with TT tube:
- Explain the procedure
- Do adequate suctioning
- Cuff deflation
- Fenestrated tracheostomy tubes or double lumen tracheostomy tube
- One-way speaking valve if the patient is comfortable
- Make a multidisciplinary team for tracheostomy care
- Tracheostomy care is a multidisciplinary approach involving trained personnel such as an intensivist, a surgeon, a respiratory therapist, a speech–language pathologist, and a clinical nurse specialist to minimize tracheostomy-related complications and better long-term care.
- The multidisciplinary team assesses the patient’s ability to tolerate a speaking valve and other augmentative communication strategies.
- Intensive care unit should have their own tracheostomy care protocol, which is subdivided into immediate, intermediate, and long-term care.

Check list for tracheostomy care in ICU and afterward:
- Always keep tracheostomy replacement kit on bedside of the patient.
- Always keep ready an intubation set in case of tube blockage.
- Patency of tube should be checked in each duty shift.
- Strict nontraumatic aseptic suction as and when required.
- Tube position should be always central.
- Avoid tube moment and traction due to ventilator circuit.
- If tube is sutured, always keep a surgical blade on bedside.
- Never send the patient with sutured tracheostomy tube out of ICU.



NOTE
Never use a speech valve when the cuff is inflated if there is no fenestration on the tube.

Fig. 47.9 Fenestrated tube and speaking valve

- Cuff pressure should be checked in every shift and maintain between 20 and 25 cmH_2O.
- Change tube only if it is blocked (partial or complete) not routinely.
- Daily care should involve stoma care/dressing, watch on bleeding infection, dryness, or granulation tissue formation.
- Protocol to decannulate should be based on, as and when patient gets better, is able to swallow, cough and there is (10–15%) air leak around deflated cuff.
- Always be suspicious for tracheal stenosis and tracheomalacia in patient where tracheostomy has been in situ for more than 3 weeks and is difficult to decannulate.

Suggested Reading

American Association for Respiratory Care; Restrepo RD, Walsh BK. Humidification during invasive and noninvasive mechanical ventilation: 2012. Respir Care. 2012;57:782–8. https://doi.org/10.4187/respcare.01766. PMID: 22546299.

Cerpa F, Cáceres D, Romero-Dapueto C, Giugliano-Jaramillo C, Pérez R, Budini H, Hidalgo V, Gutiérrez T, Molina J, Keymer J. Humidification on ventilated patients: heated Humidifications or heat and moisture exchangers? Open Respir Med J. 2015;9:104–11. https://doi.org/10.2174/1874306401509010104. PMID: 26312102; PMCID: PMC4541464.

Complications in the Intensive Care Unit. Crit Care Nurse. 2013;33(5):18–30.

Dempsey GA, Morton B. Long-term outcome following tracheostomy in critical care: a systematic review. Crit Care Med. 2016;44(3):617–28. *A systematic review of long-term outcome of surgical versus percutaneous tracheostomy*.

Hazelton JP, Orfe EC. The impact of a multidisciplinary safety checklist on adverse procedural events during bedside bronchoscopy-guided percutaneous tracheostomy. J Trauma Acute Care Surg. 2015;79(1):111–5.

Trouillet JL, Collange O, Belafia F, Blot F, Capellier G, Cesareo E. Tracheostomy in the intensive care unit: guidelines from a French expert panel. Ann Intensive Care. 2018;8:37.

Thoracentesis

48

Aakanksha Chawla, Rajesh Chawla, and Lalit Singh

Case Vignette

A 65-year-old diabetic male patient was admitted to the hospital with severe community-acquired pneumonia and respiratory failure. He was started on antibiotics and other supportive medication. On the second day of admission, his breathlessness increased and he became hypoxic despite oxygen therapy. His chest X-ray showed blunting of the right costophrenic angle. USG's chest showed the presence of 400 mL of pleural fluid on the right side.

Thoracentesis is the aspiration of fluid or air from pleural space. Thoracentesis is a percutaneous procedure where pleural fluid is removed either through a needle (typically for small volumes, e.g., <50 mL) or a small bore catheter. This can be done with or without ultrasound guidance; however, ultrasound guidance is preferred in critically ill patients.

Bedside ultrasonography can be used before the procedure to determine the presence and size of pleural effusion, assess for loculations, and to guide needle placement.

A very small free-flowing pleural effusions with less than 1 cm distance from the pleural fluid line to the chest wall on a decubitus chest radiograph has been considered too small to justify thoracentesis because of the low diagnostic yield and high risk of pneumothorax.

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With ultrasound-guided thoracentesis, the "safe window" for thoracentesis has been considered as a point where maximum pleural fluid depth is >1 cm adjacent to the parietal pleura.

Step 1: Assess the Need for Thoracentesis

Diagnostic:

- Any undiagnosed pleural effusion of any amount

Therapeutic:

- Massive pleural effusion and the patient in respiratory distress
- Suspected hemothorax
- Suspected parapneumonic infection and empyema
- Small unresolved pneumothorax

Step 2: Rule Out Contraindications

- No absolute contraindications
- Relative contraindications include the following:
  - Uncorrected bleeding diathesis
  - Chest wall cellulitis at the site of puncture
  - Lack of expertise

Step 3: Arrange All Equipment

- A thoracentesis device (This typically consists of an 8F catheter over an 18-gauge, 7.5-in. (19-cm) needle with a three-way stopcock and, ideally, a self-sealing valve.)
- A self-assembled device, if the thoracentesis device is unavailable (It includes using an 18-gauge needle or 12- to 14-gauge intravenous cannula connected to a 50-mL syringe through stopcock.)
- Injection needles—18, 20, 22, and 25 gauge
- Syringes—5, 10, and 50 mL
- A tubing set
- Antiseptic (preferably, 2% chlorhexidine solution)
- Lidocaine 1% or 2% solution
- The specimen cap for the 60-mL syringe
- Heparin 1000 IU
- Specimen collecting vials or vacutainers
- A drainage bag or vacuum bottle
- Drape (24 in. × 30 in.)

- Sterile towels
- Adhesive dressing (7.6 cm × 2.5 cm)
- Gauze pads (4 in. × 4 in.)

Step 4: Place the Patient in the Proper Position

- Ensure proper written consent of the patient or surrogate.
- Collect equipment, as well as pre-procedure diagnostic laboratory studies, as necessary.
- Alert and cooperative patients are most comfortable in a seated position leaning slightly forward, resting their head on their arms on a pillow, which is placed on an adjustable bedside table.
- This position facilitates access to 6–9th rib space in the posterior axillary line, which is the most dependent part of the thorax.
- Unstable patients and those who are unable to sit up may be in the supine position for the procedure with slight head elevation.
- The patient is moved to the extreme side of the bed, the ipsilateral hand is placed behind the head, and a towel roll is placed under the contralateral shoulder to facilitate dependent drainage.

Step 5: Procedure

1. *Needle thoracentesis.*
    - This procedure is preferably done for diagnostic pleural aspiration.
    - Position the patient appropriately as already discussed.
    - After positioning the patient and prior to preparing, ideally perform ultrasonography to confirm the pleural effusion, assess its size, look for loculations, and determine the optimal puncture site.
    - Determine the optimal puncture site by searching for the largest pocket of fluid superficial to the lung. Ideally, puncture site with sufficient pleural fluid depth (typically >10 mm) should be selected to avoid lung injury.
    - Mark the site with a needle cap, memorize the angle and depth of penetration, and anesthetize the skin and ribs.
    - If an ultrasonography machine is not available, then identify the correct site of aspiration as a site of maximum dullness on percussion of the chest.
    - Ideally, the site is between the seventh and ninth rib spaces in the middle and posterior axillary line.
    - Use standard aseptic technique for the remaining steps of the procedure.
    - Clean a wide area with an antiseptic bacteriostatic solution such as chlorhexidine.
    - Place a sterile drape over the puncture site and use sterile towels on the bed to establish a large sterile field within which to work.

- Lidocaine 2% solution should be used for local anesthesia. The skin, subcutaneous tissue, rib periosteum, intercostal muscle, and parietal pleura should all be well infiltrated with local anesthetics.
- The needle is inserted into the periosteum of the lower rib and is moved up and over the lower rib with frequent injection of small amounts (0.1–0.2 mL) of lidocaine.
- Once this needle is superior to the rib, it is slowly advanced toward the pleural space with aspiration, followed by the injection of 0.1–0.2 mL of lidocaine every 1–2 mm.
- As soon as pleural fluid is aspirated through this needle into the syringe containing lidocaine, the needle should be withdrawn from the pleural space and reattached to a 50- to 60-mL syringe through a stopcock.
- The same needle or large needle (20 gauge) is reintroduced along the same tract slowly with constant aspiration until pleural fluid is obtained.
- Aspiration is then continued until the syringe is filled with pleural fluid.
- Avoid draining more than a liter in one sitting.
- Stop aspirating if the patient coughs and gets dyspneic.
- The needle is then withdrawn, and the procedure is stopped.
- Carefully remove the needle and dress the wound.
- Label the pleural fluid and send it for diagnostic analysis.
- If the effusion is small and contains a large amount of blood, place it in an anticoagulant (heparin) so that it does not clot.
- Reposition the patient appropriately based on his or her comfort and respiratory status.
- Write a procedure note and comment specifically on the descriptive characteristics of the pleural fluid.

2. *Thoracentesis with intravenous cannula.*
    - Follow the similar procedure as pleural aspiration with the needle up to anesthetizing the desired intercostal space.
    - Then, arrange a 12G intravenous cannula with a needle and a three-way stopcock and 50-mL syringe.
    - While aspirating, introduce this cannula with the same track up to the pleural space till pleural fluid fills in the syringe.
    - Remove the inner needle from the outer cannula and reattach the three-way stopcock and syringe.
    - Then using the manual syringe pump method or vacuum bottle, aspirate the desired amount of fluid. Follow the rest of the steps as described above.
3. *Thoracentesis with commercial kits*
    - Follow a similar procedure as pleural aspiration with the needle up to anesthetizing the desired intercostal space.
    - Initially, nick the skin with a No. 11 scalpel blade to reduce skin drag.
    - While aspirating, advance the device over the superior aspect of the lower rib until pleural fluid is obtained.

- When a free flow of fluid is encountered, the catheter is advanced through the needle into pleural space approximately 1 cm and the needle is withdrawn completely.
- There is a self-sealing valve so that air does not leak into the pleural space when the needle is withdrawn; however, the needle cannot be reinserted through the catheter.
- Using either a syringe pump method or a vacuum bottle, drain the pleural effusion until the desired volume has been removed for symptomatic relief or diagnostic analysis.

Step 6: Manage Complications

Major complications:

- Pneumothorax (3–11%)
  - Pneumothorax is the most common complication of thoracentesis, occurring in <3% of cases with ultrasound guidance and up to 30% without it.
  - Ultrasound reduces pneumothorax risk, particularly in real-time guidance (0.63% vs. 4.43%), with rates lower in nonventilated patients than ventilated ones.
  - Pneumothoraces are typically small and self-resolving, but larger or symptomatic cases may require tube thoracostomy, especially in ventilated patients.
  - Risk increases with larger fluid drainage volumes (>2.3 L) and technical errors, such as incorrect needle depth or angle.
- Tension pneumothorax
- Hemothorax (0.8%)
- Laceration of the artery, liver, or spleen (0.8%)
- Diaphragmatic injury
- Empyema
- Hypotension
- Reexpansion pulmonary edema

Minor complications:

- Pain (22%)
- Dry tap (13%)
- Cough (11%)
- Subcutaneous hematoma (2%)
- Subcutaneous seroma (0.8%)
- Vasovagal syncope
- Tumor seeding

Step 7: Send Pleural Fluid for the Laboratory Tests

Routine investigations:

- Biochemical analysis—pH level (in heparinized syringe), glucose levels, protein levels, albumin, lactic acid dehydrogenase levels, adenosine deaminase, and cholesterol
- Microbiology examination—Gram stain, fungal stain and culture, AFB stain and culture, aerobic culture, and CBNAAT for *Mycobacterium tuberculosis*
- Total cell count and differential cell count
- Cytology

Special investigation based on suspected or diagnosed underlying etiology:

- Creatinine levels and pH for urinothorax
- Amylase levels—if there is a pretest suspicion of acute pancreatitis, chronic pancreatic disease, or esophageal rupture
- Triglyceride levels for chylothorax
- Hematocrit levels for hemothorax

Reasons for Dry Tap:

- Skin indentation artifact
- Skin movement artifact
- Poor angle replication
- Patient movement
- Needle blockage
- Visceral pleural impingement
- Unexpandable lung
- Inappropriately short needle

Suggested Reading

Branca P, Rodriguez RM, Rogers JT, et al. Routine measurement of pleural fluid amylase is not indicated. Arch Intern Med. 2001;161:228–32. *Pleural fluid serum amylase levels can be measured only if there is a pretest suspicion of acute pancreatitis, chronic pancreatic disease, or esophageal rupture.*

Cantey EP, Walter JM, Corbridge T, Barsuk JH. Complications of thoracentesis: incidence, risk factors, and strategies for prevention. Curr Opin Pulm Med. 2016;22:378. *This article describes complications of thoracocentesis and their prevention.*

Celik B, Sahin E, Nadir A, Kaptanoglu M. Iatrogenic pneumothorax: etiology, incidence and risk factors. Thorac Cardiovasc Surg. 2009;57(5):286–90. *At training hospitals, the incidence of* Iatrogenic pneumothorax *(IPnx) will increase in parallel to the increase in invasive procedures. Invasive procedures should be performed by experienced personnel or under their supervision when risk factors are involved.*

Conner BD, Lee YCG, Branca P, et al. Variations in pleural fluid WBC count and differential counts with different sample containers and different methods. Chest. 2003;123:1181–7. *The WBC counts obtained manually and with the automated counter from pleural fluid samples in EDTA tubes correlated very closely. The pleural fluid WBC count was lower if the pleural fluids had been collected in tubes without an anticoagulant.*

Duncan DR, Morgenthaler TI, Ryu JH, Daniels CE. Reducing iatrogenic risk in thoracentesis: establishing best practice via experiential training in a zero-risk environment. Chest. 2009;135(5):1315–20. *An improvement program that included simulation, ultrasound guidance, competency testing, and performance feedback reduced iatrogenic risk to patients.*

Porcel JM. Tuberculous pleural effusion. Lung. 2009;187(5):263–70. *A review article on the management of tubercular pleural effusion.*

Chest Tube Placement

49

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and Aakanksha Chawla

Case Vignette

A 60-year-old male patient—a known case of chronic obstructive pulmonary disease—was admitted to the hospital with sudden onset of breathlessness. On examination, he was found to be tachypneic and had cyanosis. His chest skiagram showed pneumothorax on the right side.

A chest tube placement (tube thoracostomy) is a method to insert a flexible, hollow tube into pleural space to extract air, fluid blood, or pus. It helps in maintaining negative intrapleural pressure and expansion of the lung.

Step 1: Assess the Need of Chest Tube Insertion

- Pneumothorax in any mechanically ventilated patient
- Pneumothorax after initial relief with needle aspiration
- Bilateral pneumothoraces
- Persistent or recurrent pneumothorax after simple aspiration
- Large secondary spontaneous pneumothorax

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- Malignant pleural effusion
- Empyema and complicated parapneumonic pleural effusion
- Traumatic hemopneumothorax
- Chylothorax
- Postoperative—for example, thoracotomy, esophagectomy, and cardiac surgery

Step 2: Rule Out Contraindications

There is no absolute contraindication in emergency situation:

- Bleeding diathesis (prothrombin time or partial thromboplastin time more than two times normal, platelets <50,000/mL) should be corrected in nonemergency settings.
- Inability to aspirate pleural fluid or air to confirm correct pleural space before chest drain insertion.
- Caution is required when there is a history of thoracic surgery or pleurodesis on the side of proposed chest tube insertion.
- The lung densely adherent to the chest wall throughout the hemithorax is an absolute contraindication to chest drain insertion.

Step 3: Pre-Drainage Risk Assessments

- Risk of hemorrhage, any coagulopathy, or platelet defect should be corrected prior to chest drain insertion in nonemergency situations.
- Routine measurement of the platelet count and prothrombin time is only recommended in patients with known risk factors.
- A careful radiological differentiation between pneumothorax and bullous disease, collapse and a pleural effusion, is required.
- The drainage of a postpneumonectomy space should only be carried out by or after consultation with a cardiothoracic surgeon.
- For patients with penetrating thoracic trauma, recommendation is to administer prophylactic antibiotics before chest tube placement. Patients with penetrating trauma have significantly decreased rates of empyema and pneumonia when given antibiotics before chest tube placement, as compared with placebo.

Step 4: Preparation

- Sterile gloves and gown
- Skin antiseptic solution, for example, Betadine or chlorhexidine in alcohol
- Sterile drapes, eye protection, mask, and caps
- Gauze swabs
- Intravenous catheters, tubing

- Supplemental oxygen
- Monitors (cardiac, pulse oximeter)
- A selection of syringes and needles (16–25 gauge)
- Local anesthetic, for example, lignocaine (lidocaine) 1% or 2%
- Scalpel and #10 or #15 blade
- Suture (e.g., “1–0” silk)
- Instrument for blunt dissection (e.g., curved clamp)
- Forceps and the needle holder
- The guidewire with dilators (for intercostal drainage catheter placement)
- Chest tube (No. 24–40 French)
- Connecting tubing
- Closed drainage system (including sterile water if underwater seal being used)
- Dressing and adhesive
- Antiseptic ointment
- Resuscitation cart
- Drugs—benzodiazepine, anticholinergics

Step 5: Consent and Premedication

- Written and informed consent should be taken before doing the procedures.
- Intravenous analgesics or mild sedation (benzodiazepine or narcotic) and anticholinergics should be administered.

Step 6: Patient Position

- The preferred position for drain insertion is the patient lying on the bed with the head up, slightly rotated, with the arm on the side of the procedure behind his/her head to expose the axillary area.
- Procedure can also be done while the patient is sitting upright leaning over an adjacent table with a pillow or in the lateral decubitus position.
- For most adults, place the patient in the supine position with the ipsilateral arm abducted and the elbow flexed to position the hand comfortably over the patient’s head.
- In the absence of trauma necessitating spine immobilization, the head of the bed can be slightly raised for comfort.

Step 7: Site Selection

- Careful identification of the correct patient, correct side, and correct site should be checked immediately before the procedure. Confirm the indication of chest tube insertion by reviewing the clinical signs and the chest radiograph.

- Ultrasonography can be used as adjunctive guides to the site of tube placement. Ultrasound can localize a fluid collection and image the lung to help prevent lung laceration during tube placement.
- For pleural fluid drainage, the proposed site of chest tube insertion can be confirmed by first performing a thoracentesis using ultrasound guidance. If air or fluid is not obtained during diagnostic thoracentesis, the insertion site is reassessed by reviewing the available chest radiographs or computed tomography. Occasionally, fluid may not be able to be aspirated with a small needle because of high viscosity of the pleural fluid.
- A chest radiograph must be available at the time of drain insertion except in the case of tension pneumothorax.
- The chest tube should be inserted in the fourth to sixth intercostal space in the midaxillary line in the safe triangle.
- The safe triangle is bordered by the anterior border of the latissimus dorsi, the lateral border of the pectoralis major muscle, a line superior to the horizontal level of the nipple, and an apex below the axilla.
- This position minimizes risk to underlying structures such as the internal mammary artery and avoids damage to muscle and breast tissue resulting in unsightly scarring.
- A more posterior position may be chosen if suggested by the presence of a loculated effusion or air. While this is safe, it is not the preferred site as it is more uncomfortable for the patient to lie down after insertion and there is a risk of the drain kinking.
- For apical pneumothoraces, the second intercostal space in the midclavicular line is sometimes selected but is not recommended routinely as it may be uncomfortable for the patient and may leave an unsightly scar. This site can be chosen for needle thoracostomy in tension pneumothorax.
- In hemodynamically unstable patients in whom there is a high suspicion for tension pneumothorax, needle thoracostomy in second space in the midclavicular line or fifth intercostal space should be performed as a life-saving (albeit temporizing) measure by reducing the intrapleural pressure and restoring venous return to the heart. Following needle decompression of the chest, a thoracostomy tube using a standard technique should be placed as soon as possible because needle thoracostomy may not completely relieve the tension pneumothorax and technical issues may lead to recurrent tension pneumothorax.

Step 8: Select the Drain Size

Drain size depends on the underlying pathology:

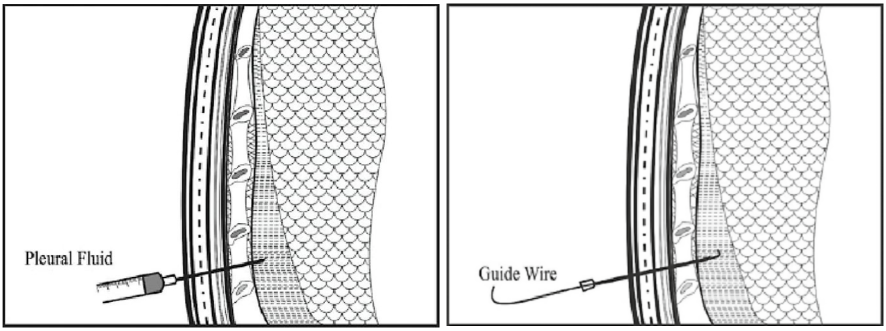
- Small-bore drains around 14 Fr to 20 Fr are recommended as they are more comfortable than large-bore tubes, but there is no evidence that either is therapeutically superior. These are put in patients with pneumothorax or pleural effusion.
- Large-bore drains of more than 24 Fr are recommended for drainage of acute hemothorax and empyema.

Step 9: Procedure

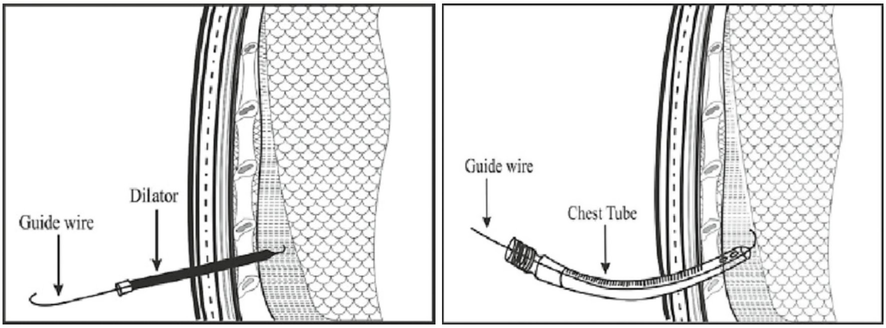
Four methods are described as follows:

1. Guidewire tube thoracostomy
2. Trocar tube thoracostomy
3. Operative tube thoracostomy
4. Single-port thoracoscopy

A. *Guidewire tube thoracostomy* (Figs. 49.1, 49.2, 49.3, and 49.4)
  - Explain the procedure to the patient.
  - Take written consent.
  - Give proper position to the patient.
  - Wear the cap and mask, perform hand hygiene, and wear personal protective equipment (PPE) with sterile gloves.
  - Provide supplemental oxygen, secure intravenous access, and attach all monitors.
  - Ensure adequate lighting.
  - Arrange all equipment on a sterile workplace.
    - Clean the skin of the patient with 2% chlorhexidine in alcohol preparation.
    - Give a frictional scrub in a circular manner to at least 10 cm area from the insertion site.
    - The field can be draped using towels. In all invasive procedures, meticulous care should be taken to minimize the risk of infection.
    - After locating intercostal space, infiltrate local anesthesia into the skin raising the cutaneous wheel at the incision site and subcutaneous tissue.
  - Anesthetize rib and pleural space in selected intercostal space.
  - Insert the introducer needle just superior to the appropriate rib. Stop just at the point where air or fluid is aspirated (Fig. 49.1).



Figs. 49.1 and 49.2 Guidewire tube thoracostomy



Figs. 49.3 and 49.4 Guidewire tube thoracostomy

- Remove the syringe keeping the needle in situ, covering the needle opening with fingers to prevent entry of air.
- Introduce the guidewire through the needle into the pleural space and then remove the needle from the pleural space while keeping the guidewire in situ (Fig. 49.2).
- Make a small nick at the entry site to allow the introduction of dilators and the chest tube.
- Use dilators to dilate the tract over the guidewire (Fig. 49.3).
- Introduce the chest tube over the guidewire into the pleural space. Confirm that all openings are in pleural space. Remove wire (Fig. 49.4).
- Connect the chest tube to the drainage system.
- Suture the tube in place and dress with gauze and tape.

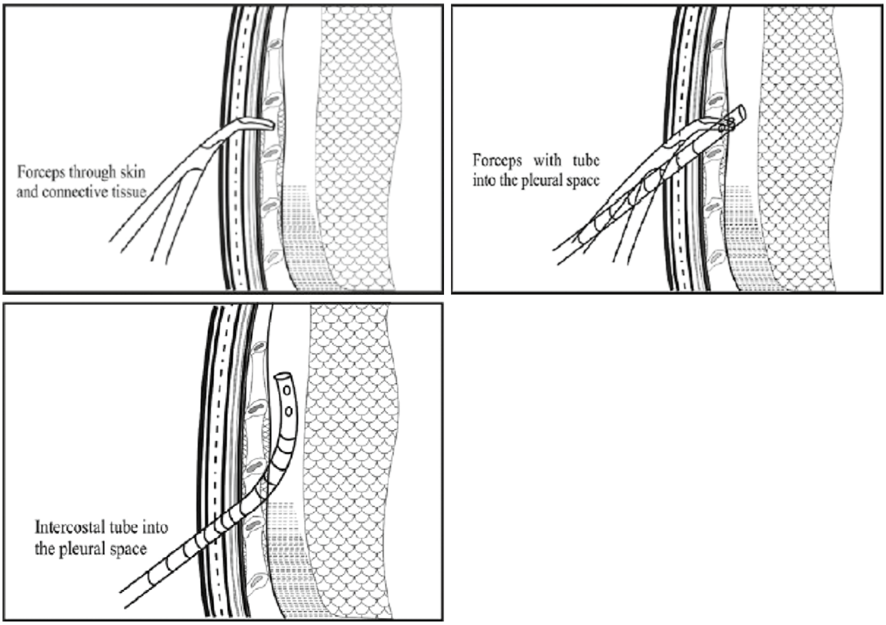
B. *Trocar tube thoracostomy*

- Take written consent.
- Give local anesthesia with 2% xylocaine.
- This method initially requires a 2–4-cm incision parallel to the superior border of the lower rib through the skin and subcutaneous tissues after local anesthesia.
- This method uses a chest tube with a trocar positioned inside the tube.
- The chest tube with the trocar can then be inserted between the ribs into the pleural cavity, directed toward the opposite shoulder with the flat edge of the stylet tip cephalad to prevent damage to the intercostal vessels.
- Because significant force is often required to insert the trocar, the hand not applying the force should be placed next to the patient's chest wall to control the depth of penetration.
- Once the pleural cavity is entered, the inner trocar is gradually removed from the chest tube. When the proximal end of the trocar clears the chest wall, a clamp is placed between the trocar and the chest wall until the trocar can be completely withdrawn and the tube attached to a water-seal drainage system.
- In critically ill patients, one should avoid the trocar tube thoracostomy.

C. *Operative tube thoracostomy*
- Explain the procedure.
- Position the patient in a semirecumbent position with the head and shoulder about 30° off the bed.
- The ipsilateral arm is placed above the head for exposure of the axilla and to increase distance between the ribs.
- Follow the first few steps as in the guidewire method.
- After locating intercostal space, infiltrate local anesthesia into the skin raising the cutaneous wheel at incision site and subcutaneous tissue.
- Generously anesthetize parietal pleura and confirm entry into pleural space by aspiration of air or fluid. Then, withdraw syringes and needles.
- Make a skin incision above and parallel to the upper border of the lower rib, one space below the desired site, in intercostals space wide enough to insert a finger.
- The incision should be made down to the fascia overlying the intercostal muscle. This fascia is then incised throughout the length of the incision, with care taken not to cut the muscle.
- Once the fascia has been incised, the muscle fibers are spread with a blunt-tipped hemostat tracking upward until the upper desired intercostal interspace is identified. This will make a tunnel, which helps in keeping the tube in the right place (Fig. 49.5).
- An incision is made in the intercostal fascia just above the superior border of the rib over which the tube will pass.
- Again, infiltrate muscle and pleura with the local anesthetic agent.
- Advance the needle into the pleural space while aspirating fluid or air to confirm the correct location.
- The parietal pleura is then dissected with a blunt-tipped hemostat, ensuring that the tip of the hemostat remains on the superior aspect of the lower rib. The hole is then enlarged by means of the operator's index finger.
- At this time, the operator should palpate the adjacent pleural space to detect any adhesions in the pleura.
- Clamp the end of the chest tube with a Kelly clamp and guide it into the pleural space with its distal end clamped. Direction is anteroapical for air and inferoposterior for fluid drainage (Figs. 49.6 and 49.7).
- Attach to the external drainage system.
- Suture the tube securely with a purse-string suture to prevent tube displacement.
- Use occlusive gauze to seal the skin around the tube.
- Dress area with a generous amount of gauze and tape.

D. *Single-port thoracoscopy*

Chest tubes can be inserted through a single-port thoracoscopy. Then under direct visualization, the chest tube is placed into the costodiaphragmatic gutter or in the upper part of thoracic cavity.


Forceps through skin and connective tissue
Forceps with tube into the pleural space
Intercostal tube into the pleural space

Figs. 49.5, 49.6, and 49.7 Operative tube thoracostomy

The great advantage is the visualization of the place where the tube will be placed.

Step 10: Verification of Chest Tube Placement

- After the chest tube has been inserted and connected to a drainage system, a chest radiograph should be obtained to verify the correctness of its position.
- Ideally, both a posteroanterior view (PA) and a lateral view should be obtained because certain ectopic locations may not be apparent on the PA view alone.
- A CT scan should be obtained when the chest tube does not drain adequately and the chest radiograph is noncontributory.
- With CT, the tube can be visualized over its entire course with accurate location. If there are undrained locules of fluid, additional chest tubes can be inserted.

Drainage System

WET and DRY systems are equally good.

One-bottle collection system:

- This system consists of one bottle that serves as both a collection container and a water seal.
- The chest tube is connected to a rigid straw inserted through a stopper into a sterile bottle.
- Enough sterile saline solution is instilled into the bottle so that the tip of the rigid straw is approximately 2 cm below the surface of the saline solution.
- The bottle's stopper must have a vent to prevent pressure from building up when air or fluid coming from the pleural space enters the bottle.
- This one-bottle system works well for uncomplicated pneumothorax.
- If a substantial amount of fluid is draining from the patient's pleural space, the level of fluid will rise in the one-bottle system, and therefore, the pressure will have to be higher and higher in the rigid straw to allow additional air or fluid to exit from the pleural space. So, in such a case, a two-bottle collection system is advised.

Two-bottle collection system **(Fig. 49.8):**

- This system is preferred to the one-bottle collection system when substantial amounts of liquid are draining from the pleural space.
- With this system, the bottle adjacent to the patient acts as a collection bottle for the drainage, and the second bottle provides the water seal and the air vent.
- The degree of water seal does not increase as the drainage accumulates. The water-seal bottle functions identically in both the one- and two-bottle systems.

Suction and three-bottle collection systems **(Fig. 49.9):**

- Controlled amounts of suction (usually 15–20 cm H_2O) can be readily applied to the system if a third bottle, the suction-control bottle, is added to the system.
- The amount of negative pressure in the system is equal to the depth to which the rigid straw in the suction-control bottle is submerged below the surface of water.

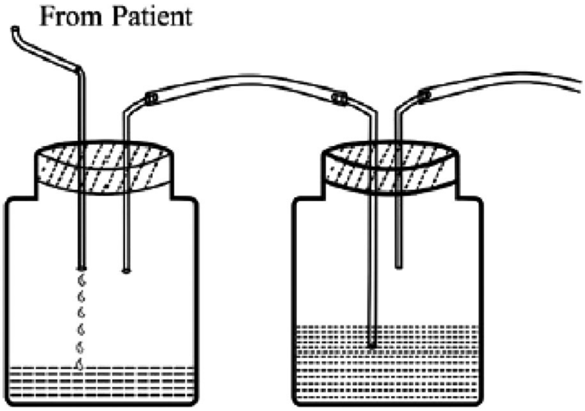


Fig. 49.8 Two-bottle drainage system

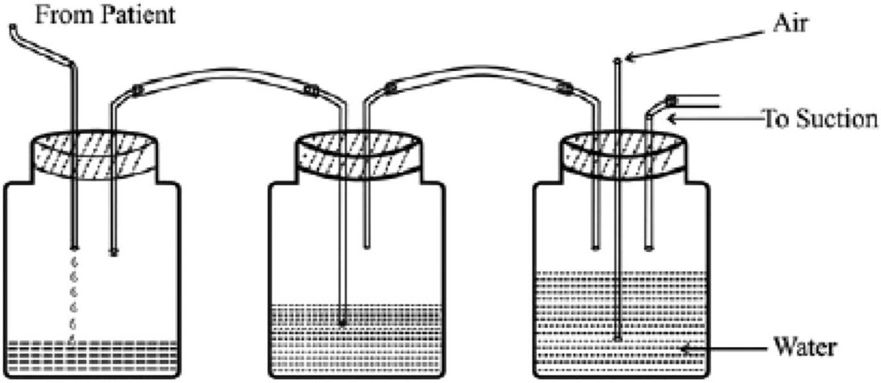


Fig. 49.9 Three-bottle drainage system

- It is desirable to apply negative pressure to the pleural space to facilitate the reexpansion of the underlying lung or to expedite the removal of air or fluid from the pleural space.

Closed-drainage suction levels: Commercial systems typically allow suction between 0 and −40 cm H_2O, with −10 to −20 cm H_2O commonly used. Suction levels vary by indication:

- For spontaneous air leaks, use minimal suction up to −10 cm H_2O to maintain lung expansion; add or increase suction if pneumothorax persists, as per chest X-ray.
- For fluid drainage, start at −20 cm H_2O and increase to achieve lung expansion, but avoid high suction if the lung is trapped.
- If the fluid is fully drained and no air leak is present, do not increase suction further.

Step 11: Care of the Chest Tube

Always see the following things:

- Is there bubbling through the water-seal bottle or the water-seal chamber on the disposable unit?
- Is the tube functioning? Always check for air column movement.
- What is the amount and type of drainage from the tube?
- If a closed-suction system disconnects, clean the tube with antiseptic (e.g., alcohol or povidone-iodine) and reconnect. If a new system is available, use it and discard the old one. For patients with an air leak, do not clamp the tube, as this can cause tension pneumothorax.

- If drainage stops and clotting or debris is suspected, the tube can be stripped or cleared by an experienced clinician. Avoid dislodging the tube during these maneuvers. If the tube becomes partially dislodged and exposed, do not attempt reinsertion.

Step 12: Guidelines for Removal

- Fully expanded lung
- Resolution of air leak for 24 h
- While some clinicians clamp the tube in addition to using a water seal to detect intermittent leaks. The patient should be closely monitored for signs of pneumothorax or effusion. If hemodynamic or respiratory distress occurs, the tube should be unclamped immediately.
- Repeat chest X-ray after 6 h to detect any air re-accumulation that might not be clinically evident.
- For pleural effusion, drainage less or up to 50 mL/day for 3 consecutive days.
- *In mechanically ventilated patients with pneumothorax:*
- In mechanically ventilated patients with pneumothorax, whether to maintain a thoracostomy tube or catheter is debated.
- Some advocate keeping it in place until ventilation ends, even without an air leak, while others argue for early removal to reduce infection risk. Lacking definitive studies, we prefer to remove the tube as soon as safely possible.

Step 13: How to Remove

- The chest tube should be removed either while the patient performs Valsalva maneuver or during expiration with a brisk firm movement while an assistant ties the previously placed closure suture.
- Obtain an early chest radiograph.
- Use of ultrasound in chest tube placement: Ultrasound or other imaging modalities (e.g., fluoroscopy, computed tomography) can be used to guide chest tube placement.

Step 14: Complications

- Local site bleeding
- Hematoma
- Hemothorax from intercostals vessel injury
- The tube misplaced
- The nonfunctional tube
- Laceration of the lung, liver, and heart
- Intra-abdominal placement

- Pneumothorax
- Infection-site cellulitis, track infection, empyema
- Reexpansion pulmonary edema—when there is large effusion, restrict drainage to 1.5 L and then clamp the tube and further drainage is done gradually after 1 h. If patient develops oedema, restrict fluids, give oxygen, and apply positive pressure ventilation if needed.
- Subcutaneous emphysema
- Clamping a chest tube with the presence of air leak may result in tension pneumothorax
- Persistent leak at the site of infection and around the tube

Step 15: Troubleshooting Thoracostomy Tubes

- Many times a closed-suction system becomes disconnected, the tube should be cleaned with an antiseptic (e.g., alcohol, povidone iodine), and the tubing reconnected.
- If a new closed-suction apparatus is immediately available, then the new one should be connected and the old one discarded.
- If patient has an air leak, the chest tube should never be clamped, because doing so can lead to tension pneumothorax.
- Instillation of fibrinolytic agents aids in maintaining flow or restoring flow in obstructed catheters.
- If the chest tube is no longer draining and there is a suspicion that it is full of clot or debris, the tube can be stripped or cleared of obstruction by other maneuvers. These manipulations should only be done by an experienced clinician, typically the physician who places and manages the tube.
- Care should be taken to avoid dislodging the tube during these attempts.
- A tube that has become partially dislodged and exposed to the external environment should not be reinserted.
- When you want to strip the tube, hold the chest tube near its insertion site with the one hand, compress the tube between the first and second fingers of the second hand, and gently pull toward the drainage system.
- If stripping the tube does not clear the tube and reestablish respiratory variation in the drainage system, then following maneuvers should be tried:
  - Twisting the tube 360°,
  - Pulling the tube out 1–2 cm,
  - Passing a sterile endotracheal tube suction catheter,
  - Injecting a small volume of sterile saline with a few drops of povidone-iodine,
  - Attempting to clear with a Fogarty balloon catheter.
- If all these fail to resolve the problem and the patient still has indications for thoracostomy, then a new tube should be placed.
- The nonfunctioning tube should be removed only after the correct placement of the new tube is confirmed and it is functioning properly.

Suggested Reading

Cerfolio RJ, Bass CS, Pask AH, et al. Predictors and treatment of persistent air leaks. Ann Thorac Surg. 2002;73:1727–30. *Steroid use, male gender, a large leak, a leak with a pneumothorax, and having a lobectomy are all risk factors for a persistent leak. Discharge on a Heimlich valve is safe and effective for patients with a persistent leak unless the leak is an expiratory.*

Gayer G, Rozenman J, Hoffmann C, et al. CT diagnosis of malpositioned chest tubes. Br J Radiol. 2000;73:786–90. *CT has proved to be extremely accurate in evaluating the position of a chest tube and has often provided additional valuable information with significant therapeutic impact*.

Gilbert TB, McGrath BJ, Soberman M. Chest tubes: indications, placement, management and complications. J Intensive Care Med. 1993;8:73–86. *A review article on chest tube management.*

Luketich JD, Kiss M, Harshey J. Chest tube insertion: a prospective evaluation of pain management. Clin J Pain. 1998;14:152–4. *In this study, a new protocol, including improved house staff, nursing education, premedication, proper insertion techniques, and more liberal and precise delivery of local anesthetics, allowed the goal of a painless chest tube insertion*.

Zgoda MA, Lunn W, Ashiku S, et al. Direct visual guidance for chest tube placement through a single-port thoracoscopy: a novel technique. Chest. 2005;127:1805–7. *A rigid telescope can be safely utilized to accurately place a chest tube after medical thoracoscopy through the same portal used for the pleuroscope*.

Pericardiocentesis

50

Rajesh Chawla, Vipul Roy, and Akhil Taneja

Case Vignette

A 60-year-old patient post coronary artery bypass grafting returned from the theater intubated and ventilated. He had two chest drains (routine postoperative) and on arrival to the intensive care unit, he was on 3 μg/min of noradrenaline infusion. Over the next 2 h, his drain output has increased from 50 mL/h to 200 mL/h and his noradrenaline requirement increased up to 20 μg/min to achieve a systolic blood pressure of 110 mm Hg. His current blood lactate is 7 mmol/L. There is no drain output this hour, the current BP is 90/78 mm Hg, and there is a visible swing in the arterial line trace. His central venous pressure is 22 mm Hg. His blood result showed a drop in hemoglobin from 9.8 to 6.5 g/dL.

The removal of fluid from the pericardial space is called pericardiocentesis. The abrupt fluid collection raises intrapericardial pressure, compresses the heart, and decreases cardiac output. This condition is called cardiac tamponade. Echocardiography is recommended to make an urgent diagnosis and look for diastolic collapse of the right atrium and ventricle due to cardiac tamponade. Immediate fluid aspiration is recommended in such a case.

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Table 50.1 Differentiating cardiac tamponade and constrictive pericarditis

Clinical signs	Tamponade	Constrictive pericarditis
Pulsus paradoxus	Common	Usually absent
Jugular veins		
Prominent *y* descent	Absent	Usually present
Prominent *x* descent	Present	Usually present
Electrocardiogram		
Low ECG voltage	May be present	May be present
Electrical alternans	May be present	Absent
Echocardiography		
Thickened pericardium	Absent	Present
Pericardial calcification	Absent	Often present
Pericardial effusion	Present	May or may not be present
Right ventricle size	Usually small	Usually normal
Myocardial thickness	Normal	Normal
Right atrial collapse and right ventricular diastolic collapse	Present	Absent
Exaggerated respiratory variation in flow velocity	Present	Present
CT/MRI		
Thickened/calcific pericardium	Absent	Present
Cardiac catheterization		
Equalization of diastolic pressures	Usually present	Usually present

Step 1: Assess the Patient

Assessment of a patient of excessive pericardial fluid is done clinically based on the clinical signs, ECG, and echocardiography (Table 50.1).

Step 2: Assess the Need for Needle Pericardiocentesis and Contraindications

A. *Indications*

Emergency

I. Evidence of cardiac tamponade:
   (a) Hypotension (refractory to fluid resuscitation and vasopressors)
   (b) Distended neck veins with cyanosis
   (c) Central venous pressure of more than 20 mmHg
   (d) Narrowed pulse pressure
   (e) No other explanation of hypotension (e.g., pneumothorax)

II. Penetrating injury to the chest between the nipples with shock

Elective

Purely diagnostic pericardiocentesis should be limited to selective cases:

- I. Cytologic evaluation (discriminate a bacterial, traumatic, neoplastic, or idiopathic cause)
- II. Removal of chronic pericardial effusion, which may also produce immediate clinical improvement
- III. Placement of a catheter for repeated pericardial drainage and lavage
- IV. Suspicion of purulent pericarditis

B. *Contraindications*

- (i) In patients of cardiac tamponade with shock, there are no absolute contraindications to performing pericardiocentesis. However, in conditions involving aortic dissection or postinfarction rupture of the myocardial free wall, needle pericardiocentesis is contraindicated. This is due to the risk of exacerbating the dissection or rupture by rapidly decompressing the pericardium and restoring systemic arterial pressure. In such cases, surgical management of tamponade is preferred.
- (ii) Septic pleuritis (may introduce infection into pericardial space).
- (iii) External wounds overlying the site of centesis. (The approach for the procedure can be from either side of thorax.)
- (iv) Thrombocytopenia ($<50{,}000/\text{mm}^3$), bleeding disorders, and anticoagulant therapy (for elective pericardiocentesis).

Step 3: Know the Options

1. *Needle pericardiocentesis*: It is the decompression of pericardial tamponade by needle aspiration of blood or fluid from the pericardial space.
2. *Intrapericardial catheterization*: This is a nonsurgical procedure, usually done in a catheterization laboratory under fluoroscopic or echocardiography guidance using a dilatational technique.

Step 4: Procedure

- Aggressive resuscitation measures should continue along with preparation for emergency pericardiocentesis.
- Vasopressor and inotropic support should be considered in fluid unresponsive shock.
- The required investigations include a complete hemogram, prothrombin time (PT), INR, activated partial thromboplastin time (aPTT), renal functions tests (RFT), and liver functions tests (LFT).
- Blind pericardiocentesis is no longer recommended. Echocardiography-guided procedure is safe and desirable (Table 50.2).

Table 50.2 Equipment for pericardiocentesis

Equipment for needle pericardiocentesis	Equipment for intrapericardial catheterization
Preparation of the site	*Catheter placement*
Antiseptic	6 Fr to 8 Fr dilator and introducer sheath Teflon-coated, flexible J-curved guidewire
Gauze, sterile drapes, and towels	A 35-cm flexible pigtail catheter 6 Fr to 8 Fr with multiple fenestrations (end and side holes)
Sterile gloves, masks, gowns, caps	or specific pericardial drainage set
A 5-mL or 10-mL syringe with a 25-gauge needle	
1% or 2% lidocaine (without epinephrine)	
Emergency drugs	
Procedure	*Drainage system*
No. 11 blade	A three-way stopcock
A 20-mL syringe with 10 mL of 1% lidocaine (without epinephrine)	Sterile tubing
An 18-gauge, 9-cm, thin-walled needle with the blunt tip	A 500-mL sterile-collecting bag (or bottle)
Multiple 20- and 50-mL syringes	Sterile gauze and adhesive bag (or bottle)
Hemostat	Suture material
Electrocardiogram machine	
Three red top tubes	
Two purple top (heparinized) tubes	
Culture bottles	
Postprocedure	
Suture material	
Scissors	
Sterile gauze and bandage	

A. *Percutaneous blind technique*
   1. Take written informed consent.
   2. *Patient preparation*: Monitor vital signs and attach a cardiac monitor. Keep the head of the bed elevated to approximately 45°. The patient should be placed at a comfortable height for the physician. A central venous catheter is essential for monitoring of right heart pressure and rapid infusion of saline and drugs. Invasive arterial pressure monitoring is indicated. Oxygen supplementation is essential:
      - *Localizing the entry site*: Locate the patient's xiphoid process and the border of the left costal margin using inspection and careful palpation. The needle entry site should be 0.5 cm to the (patient's) left of the xiphoid process and 0.5–1.0 cm inferior to the costal margin.
      - *Skin preparation: Strict asepsis is required with povidone-iodine preparation. Local anesthesia is required (lidocaine 2%) prior to the puncture.*
      - *Puncture: Puncture at a 45° angle to the skin with the needle toward the inferior tip of the left scapula.*
      - *Advancement*: Advance the needle posteriorly (while initially pressing the liver hard with the other hand to avoid a tear of the liver) with intermittent aspiration and injection of lidocaine through the path. Pass the tip beyond

the posterior border of the bony thorax (usually lies within 2.5 cm of the skin surface). If bone contact occurs, then walk the needle behind the posterior (costal) margin. Reduce the angle of contact to 15° once the tip has passed the posterior margin of the bony thorax, and continue in the same direction.

- Further *advancement is done with continuous aspiration. If electrocardiographic guidance is used, the sterile alligator clip is applied to the needle hub. Monitor continuous ECG throughout the procedure. Look for ST-segm*ent elevation or premature ventricular contractions (evidence of epicardial contact) as the needle is advanced.
- *End point*:
  - Advance the needle along this extrapleural path until a definite give-away is felt and fluid is aspirated from the pericardial space (usually 6.0–7.5 cm from the skin). Some patients may experience a vasovagal response at this point and require atropine intravenously to increase their blood pressure and heart rate.
  - If ST-segment elevation or premature ventricular complexes occur (i.e., the needle in contact with the pericardium), withdraw the needle toward the skin surface while aspirating, and if unsuccessful, then retry in the same way (caution is not to do any lateral motion as it can damage the epicardial vessels).
  - Collect the samples and send investigations accordingly.
- *Evidence of successful decompression*
- Decreased intrapericardial pressure to levels between −3 and +3 mmHg:
  - Fall in right atrial pressure and separation between the right and left ventricular diastolic pressures
  - Increased cardiac output
  - Increased systemic blood pressure
  - Reduced pulsus paradoxus to physiologic levels (≤10 mmHg)

Please note that these blind techniques have a high incidence of morbidity and mortality, and they are no longer justified without echocardiography.

B. *Echocardiography-guided intrapericardial catheterization pericardiocentesis* (Figs. 50.1, 50.2, and 50.3)

- Take an informed consent.
- The patient is placed in the semireclining position, slightly rotated leftward to enhance the fluid collection in the inferoanterior part.
- Do echocardiography.
- Define the site of entry and needle trajectory. The site of needle insertion is the place where the pericardial space is closest to the probe and the fluid accumulation is maximum.
- Local site preparation is the same as that for the percutaneous blind technique.
- A straight trajectory that avoids puncture of vital organs is chosen. The site should be 3–5 cm from the parasternal border to avoid puncture of the internal mammary artery. The optimal needle trajectory has to be preimagined by the operator.

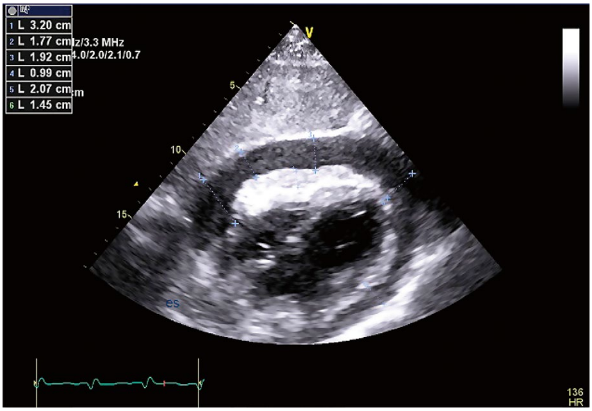
1 L 3.20 cm
2 L 1.77 cm
3 L 1.92 cm
4 L 0.99 cm
5 L 2.07 cm
6 L 1.45 cm
z/3.3 MHz
4.0/2.0/2.1/0.7
V
5
10
15
es
136
HR

Fig. 50.1 Subcostal view showing measurement of pericardial effusion

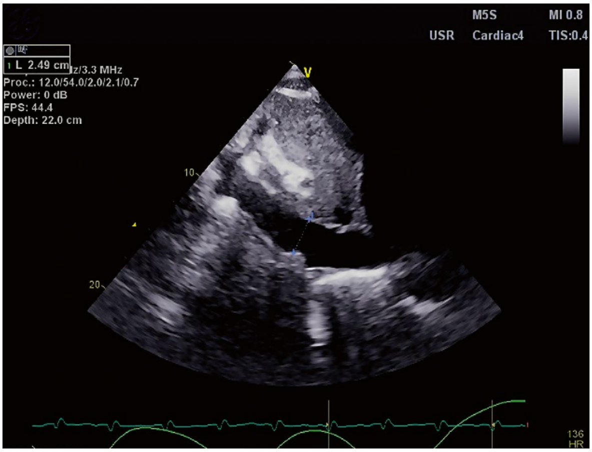
M5S
MI 0.8
USR
Cardiac4
TIS:0.4
1 L 2.49 cm
z/3.3 MHz
Proc.: 12.0/54.0/2.0/2.1/0.7
Power: 0 dB
FPS: 44.4
Depth: 22.0 cm
V
10
20
136
HR

Fig. 50.2 Dilated inferior vena cava (IVC)

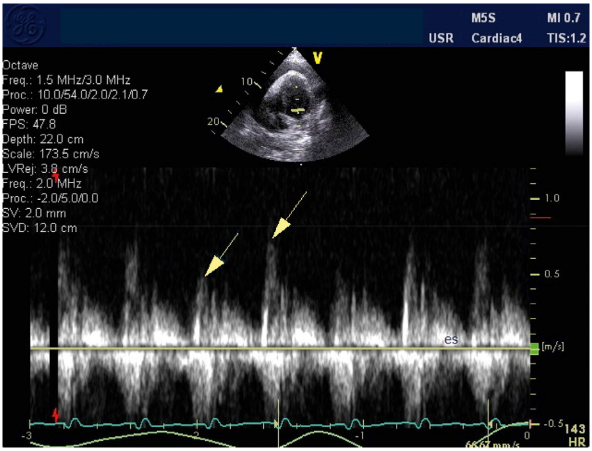
M5S
MI 0.7
USR
Cardiac4
TIS:1.2
Octave
Freq.: 1.5 MHz/3.0 MHz
Proc.: 10.0/54.0/2.0/2.1/0.7
Power: 0 dB
FPS: 47.8
Depth: 22.0 cm
Scale: 173.5 cm/s
LVRej: 3.8 cm/s
Freq.: 2.0 MHz
Proc.: -2.0/5.0/0.0
SV: 2.0 mm
SVD: 12.0 cm
V
10
20
1.0
0.5
[m/s]
-0.5
es
-3
-2
-1
0
66.67 mm/s
143
HR

Fig. 50.3 Variation of mitral inflow velocity with respiration (>25%)

- A 14–16-gauge Teflon sheath needle attached with a saline-filled syringe is used. On entering the fluid, further advancement of 2 mm is advised; the sheath is advanced over the needle and the needle is withdrawn. Confirmation of the needle position is done by 5 mL of agitated saline and seen by echocardiography in the pericardial space (Table 50.3).
- Seldinger technique is used to place a guidewire through the sheath, and then, the sheath is removed. A series of skin dilations is then performed to finally allow an 8F, 35-cm flexible pigtail catheter to be guided over the guidewire into the pericardial space.
- Maintenance of the system—secure the pigtail with suture and connect it to a reservoir. Flush the drain every 4–6 h with 10–15 mL saline to maintain the patency.
- Other different methods and kits are now available as possible alternate techniques.

C. *Fluoroscopic technique*

This is done in the catheterization lab. This was the first imaging system that was developed for percutaneous pericardiocentesis.

- This is performed via the subxiphoid approach.
- Needle containing contrast medium is directed toward the left shoulder at a 30° angle to the skin.
- Contrast medium is injected to confirm the needle in pericardial space.
- Sluggish, inferior layering of contrast medium indicates the correct position for J-tip guidewire introduction.
- Guidewire position is confirmed in at least two angiographic views (lateral and anterior–posterior).
- The rest of the procedure is the same as with echocardiographic approach
- This method is standardized and effective but requires a heart catheterization lab.
- Catheter drainage care is done by intermittently aspirating every 6 h to prevent occlusion of the catheter.

Table 50.3 Echocardiographic findings in cardiac tamponade

Views	Findings
Two-dimensional (2D) subcostal, parasternal long axis (PLAX), parasternal short axis (SAX)	Pericardial effusion (Fig. 50.1)
2D PLAX (RV collapse), Apical 4 chamber (right atrium (RA), right ventricle (RV) collapse)	Systolic collapse of RA and diastolic collapse of RV
Sub costal view	Dilated inferior vena cava (IVC) and loss of respiratory variation (Fig. 50.2)
Apical four-chamber	Increased interventricular dependence with respiration
Pulsed wave doppler (PWD)	>25% of respiratory variation in mitral inflow and tricuspid inflow (Fig. 50.3)

Step 5: Manage Complications (Table 50.4)

Table 50.4 Management of complications

	Complications	Prevention/treatment
Structural damage	Cardiac puncture with hemopericardium	Careful procedure, urgent thoracotomy, and repair
	Coronary artery laceration (hemopericardium or myocardial infarction)	Careful procedure, urgent thoracotomy, and repair
	Fistula formation	Surgical correction
Rhythm disturbance	Arrhythmias, bradycardia, ventricular tachycardia/ventricular fibrillation	Often spontaneously revert, may need cardioversion/defibrillation/cardiopulmonary resuscitation
	Cardiac arrest (precipitated by pulseless electrical activity, tachyarrhythmia, or bradyarrhythmia)	Cardiopulmonary resuscitation according to ACLS protocol
Dysfunction (cardiopulmonary)	Transient biventricular dysfunction	Often reverts, vasopressors, and inotropes
	Pulmonary edema	Manage according to standard practice
Extracardiac	Hemothorax	Intercostal tube drainage (ICD)
	Pneumothorax	ICD insertion
	Trauma to abdominal organs (liver, gastrointestinal tract)	Careful procedure, better to do under ultrasonographic or fluroscopicguidance
	Infection	Standard therapy

Step 6: Send Investigations of Pericardial Fluid (Table 50.5)

Table 50.5 Investigations of pericardial fluid

Investigations
Hematocrit
White blood cell count with differential count
Glucose, protein, cholesterol, triglyceride
Amylase, lactate dehydrogenase
Gram’s stain
Routine aerobic and anaerobic cultures
Smear and culture for acid-fast bacilli
GeneXpert for *Mycobacterium* TB
Cytology
Special cultures (viral, parasite, fungal)
Antinuclear antibody
Rheumatoid factor
Total complement, C3

Suggested Reading

Fink MP, Abraham E, Vincent JL, Kochanek PM. Pericardiocentesis. In: Textbook of critical care. 5th ed. Philadelphia: Elsevier Saunders; 2005. p. 1833–40. *Gives a comprehensive description of pericardiocentesis.*

Flint N, Siegel RJ. Echo-guided pericardiocentesis: when and how should it be performed? Curr Cardiol Rep. 2020;22(8):71. https://doi.org/10.1007/s11886-020-01320-2. *Detailed echo-guided procedure.*

Maggiolini S, Osculati G, Vitale G. Utility and safety of diagnostic pericardiocentesis. Eur Heart J. 2005;26(10):1046–104. *Stresses the view that pericardiocentesis should be performed only on a strong clinical indication, by an experienced operator with the safest technique.*

Lumbar Puncture

51

Rajesh Chawla, Charu Gauba, Sudha Kansal,
and Kirtikar Ghorela

Case Vignette
A 40-year-old male patient was admitted to the hospital with altered sensorium, headache, vomiting, high-grade fever, and rash. He was drowsy. His pulse was 120/min and blood pressure was 110/80 mmHg. Neck rigidity was positive and the CT scan report of the head was normal. A lumbar puncture (LP) was planned.

Lumbar puncture is a commonly performed procedure to obtain cerebrospinal fluid (CSF) to diagnose various neurological disorders. The indications for lumbar puncture could be diagnostic or therapeutic and these can be undertaken in urgent or non-urgent situations,

Step 1: Assess the Need for Lumbar Puncture

A. *Diagnostic indications*
   - Infectious disease
     - Meningitis
     - Tubercular
     - Viral

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  - Bacterial
  - Fungal
  - Encephalitis
- Subarachnoid hemorrhage (SAH) with negative CT scan
- Demyelinating/inflammatory diseases
  - Multiple sclerosis/acute disseminated encephalomyelitis
  - Guillain–Barré syndrome/chronic inflammatory demyelinating polyneuropathy
  - Neurosarcoid
  - Paraneoplastic syndromes
  - CNS syphilis
  - Autoimmune encephalitis
- Neurodiagnostic imaging
  - Myelography
  - Cisternography
- CSF pressure (opening pressure)
  - Normal pressure hydrocephalus (NPH)
  - Idiopathic intracranial hypertension (IIH)
- Oncologic procedures
  - Carcinomatous meningitis
  - Central nervous system lymphoma

B. *Therapeutic indications*

- Neuraxial analgesia and anesthesia
  - Narcotics
  - Local anesthetics
- Ventriculitis and post-instrumentation meningitis
  - Antibiotic administration
- Leukemias and lymphomas with cerebrospinal involvement
  - Chemotherapy
  - Methotrexate
- Draining CSF in NPH and IIH

C. *Urgent and nonurgent indications*

URGENT:

- Suspected CNS infection (except brain abscess or a para meningeal process)
- Suspected SAH in a patient with a negative CT scan

NONURGENT:

- Idiopathic intracranial hypertension (pseudotumor cerebri)
- Carcinomatous meningitis
- Tuberculous meningitis
- Normal pressure hydrocephalus
- CNS syphilis
- CNS vasculitis

D. *Conditions in which LP is rarely diagnostic but still useful include:*

- Multiple sclerosis
- Guillain–Barré syndrome
- Paraneoplastic syndromes

Step 2: Be Familiar with the CSF Analysis

Tests on CSF are determined by:

- Age
- Clinical history
- Differential diagnosis

Basic investigations:

- Biochemical
  - Glucose

    Approximately two-thirds of serum glucose or higher.

    Decreased levels below 40–50% of serum glucose generally imply a bacterial infection.

    Simultaneously random blood sugar must be checked.
  - Protein (<0.5% of plasma)

    CSF total protein: 15–45 mg/100 mL

    Approximately 1000 RBCs = 1 mg% protein (in a bloody tap)

    Increased protein
    - Infective and post-infective state
    - Demyelinating polyneuropathies
- Hematology
  - Cell counts

    Total
    - Maximum 5 WBCs/mL; RBCs nil
    - In bloody tap 1, WBC per approximately 700 RBCs can exist

    Differential
- Microbiology
  - Stains: gram/fungal/acid fast/India ink
  - Cultures: aerobic/fungal/tubercular
- Immunology
  - Cryptococcal antigen
  - Bacterial antigens
  - Viral (e.g., herpes simplex PCR)
  - Multiplex PCR
  - Mycobacterial (TB PCR)
  - Immunoglobulins
  - Oligoclonal band
  - Cysticercus antibody
  - VDRL
- Cytology
  - Malignancies

Step 3: Rule Out the Contraindications

Absolute:

- Infected skin or suspected spinal epidural abscess over the needle entry site
- Risk/signs of cerebral herniation
  - Intracranial lesions especially posterior fossa tumors
  - Intraspinal mass, especially intramedullary
  - Focal neurological signs
  - Brain stem signs
    Pupillary changes
    Decerebrate posturing
    Altered respiration

Relative:

- Raised intracranial pressure (ICP)
- Cardiorespiratory compromise: position related
- Coagulopathy/thrombocytopenia (platelet count <50,000 or INR >1.5): risk of spinal hematoma
- Previous lumbar surgery/congenital defects/degeneration: may require radiology guidance

Step 4: Order CT Head Before Lumbar Puncture

In all patients to rule out mass effect/frank bleeding, especially if there is:

- Age > 60 years
  - Immunocompromised patient with known CNS lesions
  - Altered sensorium
  - Focal neurological deficit
  - Seizure within past 1 week
  - Papilledema
  - Suspicion of raised ICP
  - Suspected metastatic cancer

CT does not always rule out the risk of herniation completely.

When the lumbar puncture (LP) is delayed or deferred in the setting of suspected bacterial meningitis, it is important to obtain blood cultures (which reveal the pathogen in more than half of patients) and promptly institute antibiotic therapy. Urgent evaluation and treatment of increased ICP, along with the administration of antibiotics and steroids, should be instituted promptly when this is suspected.

Step 5: Informed Consent

- Discuss the prognosis of the patient and the need for the procedure.
- Explain in detail the advantages and disadvantages of the procedure and the available options.
- Obtain an informed consent.

Step 6: Prepare for the Procedure

- A spinal needle (20G commonly)
- Sterile sheets and instruments
- A manometer
- Antiseptic cleansing agents, lignocaine 2%
- Numbered collection tubes (at least 4)
- Functioning intravenous access
- Crash cart
- Vital monitoring depending on the patient condition

Step 7: Position the Patient

Explain the procedure to the patient if he/she is conscious.

Take informed consent.

Lateral decubitus position:

- Preferred for an accurate opening pressure.
- Less incidence of post-puncture headache.
- Make the patient acquire a fetal position with the back flexed to widen the gap between the spinous processes.
- The head flexed, chin close to the chest.
- Hips flexed.
- Knees flexed and as close to the chest as possible.
- Keep the back perpendicular to the bed and close to the edge.
- Lumbar spine should be perpendicular to the bed, leaning forward on a bedside table (Fig. 51.1)

Sitting position:

- Preferred for obese/elderly/degenerative spine/prior back surgery.

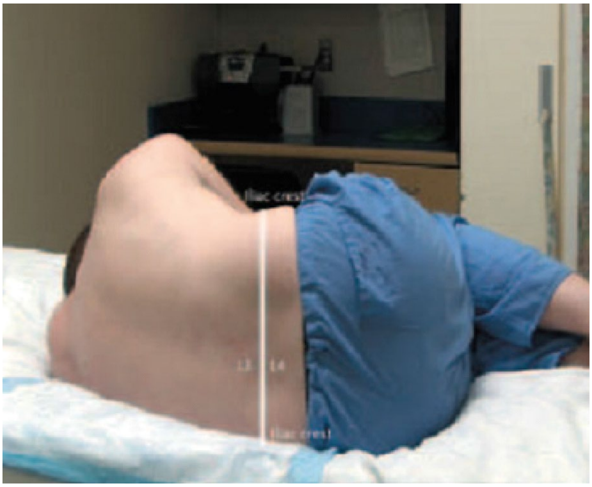

Fig. 51.1 Position for lumber puncture

Prone position:

- This is used for procedures performed with fluoroscopic guidance.

Step 8: Know Landmarks and Anatomy

Skin-marking pencils should be used to mark before skin preparation:

- Determine the superior point of iliac crests.
- Connect both crests with the imaginary line.
- This line crosses the midline at the L4 spine level (the spinal cord ends at the lower border of L1 in adults).
- The spinal needle can be safely inserted into the subarachnoid space at the L3–L4, L4–L5, or L5–S1.
- Walk the fingers down over the spinous process to palpate L4–L5 and L5–S1 interspaces.
- Layers encountered during LP are the following:
  - Skin
  - Superficial fascia
  - Supraspinous ligament
  - Interspinous ligament
  - Ligamentum flavum
  - Epidural space
  - Dura
  - Arachnoid membrane

Step 9: Procedure

- Preparation
  - Wear the cap, masks, and goggles.
  - Scrub appropriately.
  - Wear the sterile gown and gloves.
  - Prepare the skin:
    - Use povidone-iodine or chlorhexidine.
    - Cover several interspaces.
  - Drape with the sterile fenestrated sheet with the opening over the intended area.
  - Cover the iliac crest with the sheet.
- The procedure
  - Apply local anesthesia (2% lignocaine), use a 25-gauge needle, and infiltrate subcutaneously. Use a 20-gauge needle for deeper tissue and aspirate to see that no blood is aspirated before injecting. Inject while withdrawing the needle. Cover a broad area to allow manipulation.
  - Systemic sedatives and analgesics can be used under close monitoring.
  - Reconfirm the landmarks and interspaces by palpation.
  - Insert the 20- or 22-gauge spinal needle with stylet in place at superior aspect of inferior spinous process.
  - Stay in the midline.
  - Angle 15–30° cephalad; aim for the umbilicus.
  - If the needle is bevel tipped, then keep bevel in sagittal plane. Feel the layers as the needle passes through.
  - Popping sensation is felt as the needle passes through the ligamentum flavum.
  - Another feeling of giveaway is felt on puncturing the dura.
  - Feeling of the layers becomes more consistent with practice.
  - Withdraw the stylet to check for flow: if none present, rotate by 90° or advance by 2 mm and recheck.
  - If flow is poor, rotate by 90°.
  - If bone is encountered, withdraw the needle up to the subcutaneous tissue and redirect the needle superiorly or inferiorly.
  - Once the flow is adequate, do the following:
  - Measure opening pressure as the height of the fluid via the flexible tube connected to the manometer and needle hub.
  - Relax the legs for accurate measurement.
  - Measure in recumbent position only (normal pressure: 70–180 mm H_2O).
  - Collect samples and do not aspirate—it may cause hemorrhage.
  - Once minimum amount is collected, replace stylet and withdraw the needle.
  - Apply pressure at the puncture site, use tincture benzoin to seal, and apply bandage.
  - It was said to keep the patient supine for 1–3 h to reduce severity of postdural puncture headache, although a meta-analysis of 16 randomized controlled trials of LP performed for anesthesia, myelography, or diagnostic purposes

  found no evidence in any trial that longer bed rest was superior to immediate patient mobilization or shorter bedrest.
  - An alternate approach to obtaining cerebrospinal fluid (CSF) with a paramedian needle insertion through the L5–S1 space (Taylor approach) specially in patient with advanced ankylosing spondylosis.

Newer Technique

Fluoroscopic guidance for LP may be required if attempts without imaging are unsuccessful. This is also suggested for patients who are obese or have difficult anatomy because of prior spine surgery or other reasons. Most neuroradiologists perform fluoroscopically guided LPs in the L2–L3 or L3–L4 intervertebral space with the patient in the prone position and rotate the patient to their side for measurement of opening pressure. In addition to improving success rates, fluoroscopic guidance may reduce the incidence of traumatic LP.

Ultrasound guided lumbar puncture can also be performed.

Step 10: Know the Complications and Their Management

- Postdural puncture headache
  - Most common
    - Excessive CSF leak
    - Intracranial hypotension
    - Stretch on pain-sensitive veins
    - Linked to previous history of headaches and psychological factors
  - Risk decreased by
    - Thinner needles
    - Paramedian approach
    - Pencil-point needles (controversial)
    - Bevel parallel to sagittal dural fibers: to split, not cut
    - Replacing the stylet before withdrawing
  - Features
    - Typically occurs within 72 h and lasts 3–5 days
    - Increases on sitting up, better on lying down
    - Usually frontal
  - Treatment
    - Bed rest
    - Hydration
    - Analgesics
    - Methylxanthines—caffeine (most effective), theophylline
    - Epidural blood patch is most effective.
    - Epidural injection of saline, dextran, or adrenocorticotropic hormone has been described.

- Hemorrhage (uncommon)
  - More risk with bleeding tendency.
  - *Spinal SAH*: radicular pain, paraparesis, sphincter disturbances.
  - *Spinal subdural hematoma (rare)*: early surgical intervention, else irreversible neurological damage may occur.
- Difficulty in identifying landmarks or subarachnoid space
  - Obesity
  - Ankylosing spondylitis
  - Kyphoscoliosis
  - Lumbar surgery
  - Disk degeneration
  - Calcification of ligaments

  Request for an anesthesiologist or interventional radiologist.

- Dry tap
  - The misplaced needle tip
  - Dehydration
  - Low CSF volume
- Infection (uncommon)
  - Seeding of skin flora: preventable by aseptic technique
  - More risk with repeated procedures or lumbar drains
- Hemodynamic disturbances
- Cerebral/spinal herniation (see Steps 3 and 4)
  - Raised ICP
  - Cerebrospinal pressure gradient
  - Intramedullary/intracerebral mass lesions
- Hearing loss (rare)
  - Decreased ICP transmitted to cochlear apparatus
  - Reversible
  - Underreported
- Sixth nerve palsy
  - Reversible
  - Traction injury with decreased ICP
- Injury to spinal nerves
  - Usually neuropraxia
  - Local or referred pain
- Subarachnoid epidermal cysts
  - Seeding with skin tissue
  - Avoided by a needle with stylet

Step 11: Managing the Anticoagulated Patient and Timing of LP

Antiplatelets

- NSAIDs: No contraindication
- Ticlopidine: Discontinue 14 days prior
- Clopidogrel: Hold 7 days prior
- GP IIb/IIIa inhibitors: Hold 8–48 h prior

Unfractionated heparin

- Subcutaneous

  If the total dose is less than 10,000 units/day, twice daily, there is no contraindication.

  If the total dose is more than 10,000 units/day, more than twice daily, safety is not established.
- Intravenous

  One hour prior and 2–4 h after heparin dose.

  No change in next dose timing even if traumatic.

Low-molecular-weight heparin

- Therapeutic dosing
  - 24 h after the last dose
- Single daily dosing
  - 10–12 h after the last dose
  - Next dose 4 h after the procedure

Warfarin

- International normalized ratio 1.5 or less

Fondaparinux Stop 2 to 4 days before the procedure
Direct thrombin inhibitors

- Insufficient evidence should be avoided.
- If still necessary
  - 8–10 h after the last dose
  - 2–4 h after needle placement

Thrombolytics

- Absolute contraindication

For elective procedures in a patient receiving systemic anticoagulation, observational studies and expert opinion have suggested stopping the agents for a specified time period prior to spinal anesthesia or LP.

- Unfractionated intravenous heparin drips—2–4 h.
- Low-molecular-weight heparin—12–24 h.
- Warfarin—5–7 days.
- Newer oral anticoagulants (NOACs), apixaban, edoxaban, and rivaroxaban—48 h.
- Dabigatran should be held 48–96 h based on renal function.
- Subcutaneous heparin— <10,000 units/day is not believed to pose a substantial risk for bleeding.

Suggested Reading

Ellenby MS, Tegtmeyer K, Lai S, et al. Lumbar puncture. N Engl J Med. 2006;355:e12. *The article presents a simplified and structured review about lumbar puncture in a step-by-step fashion to guide a physician through its practical and diagnostic aspects.*

Fink MP. Lumbar puncture. In: Textbook of critical care. 5th ed. Philadelphia: Elsevier; 2005. p. 1885. *This textbook outlines the preparation and technique adopted for successful and safe execution of lumbar puncture in a crisp and to the point way.*

Horlocker TT, Wedel DJ, Rowlingson JC. Regional anesthesia in the patient receiving antithrombotic or thrombolytic therapy. American Society of Regional Anesthesia and Pain Medicine Evidence-Based Guidelines (3rd ed.). Reg Anesth Pain Med. 2010;35:64–101. *The basis of these recommendations is on case reports, clinical series, pharmacology, hematology, and risk factors for surgical bleeding.*

Irwin RS, Rippe JM. Cerebrospinal fluid aspiration. In: Irwin and Rippe's intensive care medicine. 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2008. p. 151. *The text outlines in detail the diagnostic and therapeutic indications of a lumbar puncture along with a review of the techniques involved and the complications one could face during the procedure.*

Website

http://emedicine.medscape.com/article/80773-overview#a01

Intra Aortic Balloon Pump

52

Khusrav Bajan

Case Vignette

A 60-year-old male patient was admitted to the emergency room with a history of chest pain for about 3 h. He was irritable, had cold extremities, and was hypotensive with a blood pressure of 84/60 mmHg. He has been a diabetic and a smoker for around 10 years. He persisted to be hypotensive despite being on adrenaline and noradrenaline. His ECG showed an extensive anterior wall STEMI. He was taken to the cardiac catheterization laboratory for a percutaneous coronary intervention (PCI) and an intra-aortic balloon pump (IABP) insertion. After 2 days, the patient's cardiogenic shock improved and was then discharged on day 7.

Although intra-aortic balloon pump (IABP) has a modest hemodynamic beneficial effect compared to novel, advanced mechanical circulatory support devices, it has a better safety profile, relative simplicity to use, and a beneficial cardiovascular physiological impact. These features make IABP a frequently used circulatory support device in patients requiring hemodynamic support either in cardiogenic shock or at risk of hemodynamic decompensation during a high-risk coronary intervention.

The IABP is a mechanical device to support cardiac pump function temporarily by increasing coronary perfusion and decreasing afterload. It augments and couterpulsates, making it useful as a salvage therapy in cardiogenic shock. IABP therapy should therefore be considered for use in patients who have the potential for left ventricular recovery or to support those awaiting cardiac transplantation. The better outcomes of IABP with concomitant PCI/thrombolysis in earlier studies led to the Class I recommendations of the use of IABP in acute coronary syndrome with cardiogenic shock.

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Though the IABP Shock II trial did not show any statistically significant difference in the 30-day mortality in the groups treated with or without IABP in patients with cariogenic shock, the real-life clinical benefits seen on hemodynamics and organ perfusion has led to the abundant use of the IABP. The IABP, as opposed to left ventricular assist device (LVAD—Impella), is easier to insert and manage. It costs less and is effective. A brief comparison of IABP with other commonly used mechanical circulatory support (MCS) devices is represented in Table 52.1.

Table 52.1 Comparison of IABP with mechanical circulatory support devices

Characteristics	IABP	Impella	TandemHeart	VA-ECMO
Availability	Widely available	Availability gradually increasing	Less commonly available	Limited
Mechanism	Counterpulsation (inflates during diastole and deflates during systole)	Direct ventricular unloading (directly unloads LV and increases coronary perfusion)	Indirect ventricular unloading (indirect LV unload achieved through atrial drainage)	Cardiopulmonary bypass (single circuit biventricular support)
Hemodynamic support delivery rate	0.5–1 L/min	2.5–5.5 L/min	Up to 4 L/min	Up to full cardiopulmonary bypass
Indications	ACS requiring CABG or complex PCI, decompensated HF	CS, complex interventions, compromised hemodynamics	CS, complex interventions	Refractory CS with biventricular failure
Placement	Femoral, axillary, or brachial arteries	Femoral artery, left ventricle	Femoral vein and artery, requires septostomy	Central or peripheral cannulation
Expected hemodynamics	Increases coronary perfusion, reduces afterload and myocardial work	Decreases LV wall stress, increases coronary perfusion, supports MAP	Decreases LV wall stress, increases coronary perfusion, supports MAP	Biventricular support, robust peripheral perfusion
Complications	Vascular access complications, limited support in cardiogenic shock	Hemolysis, device migration, bleeding	Hemolysis, bleeding, septostomy complications	Vascular access complications, bleeding, stroke, LV overload
Special requirements	None	None	Septostomy, no perfusionist needed	Dedicated perfusionist
Expertise required	Low to moderate	Moderate	High	High
Unique benefits	Does not interfere with surgical/percutaneous techniques, easily removable	Early use improves hemodynamics, no need for septostomy	Robust LV unloading, can be part of ECMO circuit	Provides biventricular support, suitable for active CPR

In order to decipher and implement the use of an IABP, one must incorporate the following steps in perspective.

Step 1: Assess the Indications for IABP Insertion

Since the balloon counterpulsation helps to improve the myocardial oxygen supply and decrease oxygen demand, the IABP is indicated for conditions with decreased myocardial oxygen supply–demand ratio. The common indication would be a systolic blood pressure <90 mmHg of cardiac origin, not responsive to other interventions.

- Cardiogenic shock not quickly reversed with pharmacological therapy
- Acute myocardial infarction with refractory pulmonary edema
- Mechanical complications of myocardial infarction (ventricular septal defect, acute mitral regurgitation)
- Unstable angina refractory to medical treatment
- In conjunction with thrombolysis in myocardial infarction
- Bridge to cardiac transplant
- Bridge to left ventricular assist devices
- Ventricular arrhythmias secondary to ischemia
- High-risk cardiac surgeries
- Patients undergoing noncardiac surgery with high cardiac risk
- Postoperative low cardiac output syndrome
- Weaning from bypass open heart surgery

Step 2: Assess the Contraindications for IABP Insertion

- *Absolute*
  - Irreversible brain damage
  - Chronic end-stage heart disease without the possibility of heart transplant
  - Dissecting aortic aneurysms
- *Relative*
  - Aortic incompetence
  - Severe peripheral vascular disease where the decision is based on patient risk–benefit ratio
  - Uncontrolled sepsis
  - Uncontrolled bleeding disorder

Step 3: Apply Principles of IABP (Fig. 52.1)

- The IABP is positioned in the descending thoracic aorta just distal to the left subclavian artery.

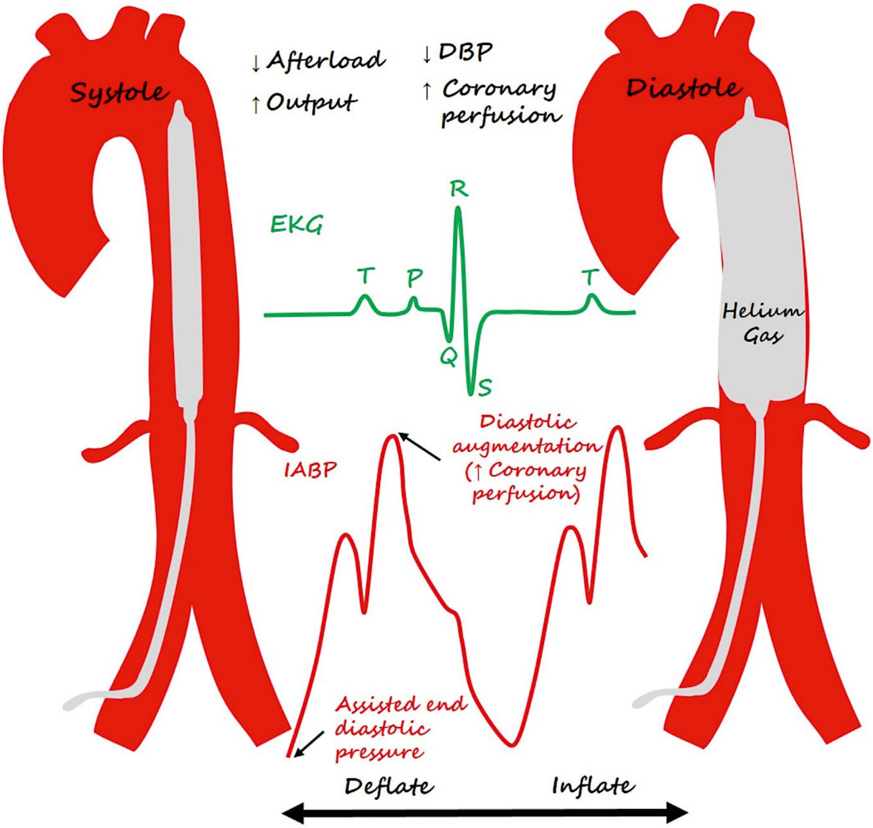
Systole
↓ Afterload
↑ Output
↓ DBP
↑ Coronary perfusion
Diastole
EKG
R
T
P
T
Q
S
Helium Gas
IABP
Diastolic augmentation (↑ Coronary perfusion)
Assisted end diastolic pressure
Deflate
Inflate

Fig. 52.1 Principles of IABP

- It is connected to an IABP console, which shuttles helium in and out of the balloon, and is timed to inflate and deflate in synchronization with the mechanical cardiac cycle; i.e., the balloon inflates during cardiac diastole and deflates during cardiac systole.
- Inflation at the onset of diastole results in proximal and distal displacement of blood volume in the aorta. This displacement creates elevated pressures by which the coronary artery and systemic perfusion is increased.
- Deflation occurs just prior to the onset of systole. This leads to reduction in the systolic pressure, thus decreasing the afterload. Myocardial oxygen demand is decreased as a result of the reduction in systolic pressure and thus improving cardiac output. This property is known as counterpulsation.

  The expected changes in cardiogenic shock after insertion of IABP would be increase in cardiac output, increase in diastolic pressure, decrease in heart rate, pulmonary wedge pressure, and variable effect on systolic pressure.

Step 4: Utilize Techniques of IABP Insertion

- It consists of two principal parts:
  - The first part is a catheter with two lumens, one for flushing and pressure monitoring and another for delivery of helium gas in a closed balloon (34–50 cc).
  - The second part is a mobile console for delivering helium (inert gas), controlling balloon inflation and deflation cycling, and displaying pressure waveforms and alarms.
- The balloon is inserted from the femoral artery using a Seldinger technique and advanced under fluoroscopic guidance.
- In rare cases, it may be inserted through the axillary artery in patients with severe peripheral arterial disease with bilateral femoral artery occlusion or graft.

Step 5: Deployment and Positioning the IABP

- The tip of the balloon should lie 2–3 cm below the left subclavian artery so that the entire length of the balloon lies in the descending thoracic aorta.
- The tip of the balloon catheter is radiopaque, and hence, a check X-ray should always be taken after insertion to ensure correct balloon placement. The tip should be at the level of bifurcation of left and right main bronchi at the level of carina.
- The balloon should not be too high to avoid blocking the branches of the arch of the aorta, especially the left subclavian artery, and should not be too low so as to avoid blocking the renal arteries.

Step 6: Set Cycling Time for IABP (Fig. 52.2)

- The mechanical cardiac cycle represented by the arterial pressure waveform is observed to assess appropriate timing.
- Electrocardiographic synchronization may also be done for cycling.
- Inflation of the intra-aortic balloon occurs at the onset of diastole noted by the dicrotic notch on the arterial waveform.
- A sharp deep “V” should be observed when the balloon inflates. As the balloon inflates, aortic diastolic pressure is augmented and a second peak is observed. This peak is referred to as diastolic augmentation.
- Diastolic augmentation (30%) is ideally higher than the patient’s systolic pressure and is generated by the displacement of blood volume within the aorta.

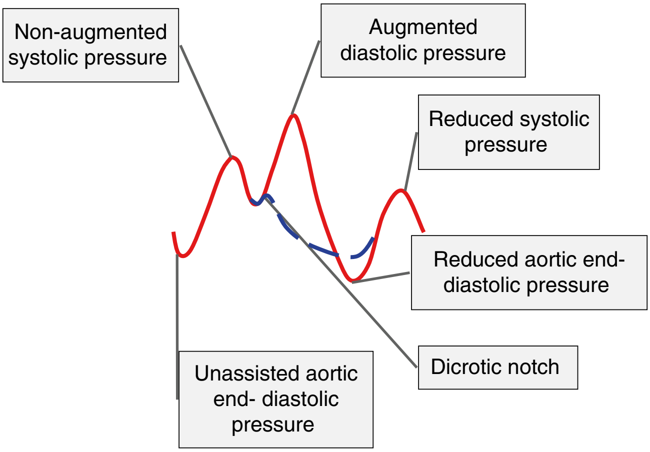
Non-augmented systolic pressure
Augmented diastolic pressure
Reduced systolic pressure
Reduced aortic end-diastolic pressure
Dicrotic notch
Unassisted aortic end- diastolic pressure

Fig. 52.2 IABP waveform

- Deflation occurs at end-diastole prior to the next systole. The precise timing of deflation is found by observing the arterial pressure tracing. The optimal deflation point is selected to achieve the greatest reduction (20%) in the next unassisted systole.
- An effective IABP cycling will result in increase of mean arterial pressure, decrease in heart rate, decrease in pulmonary capillary wedge pressure, and increase in cardiac output.
- Many consoles have an auto/semi-auto and manual modes.

Suboptimal timing of inflation and deflation of the balloon (Figure 52.3a–e) will result in hemodynamic instability.

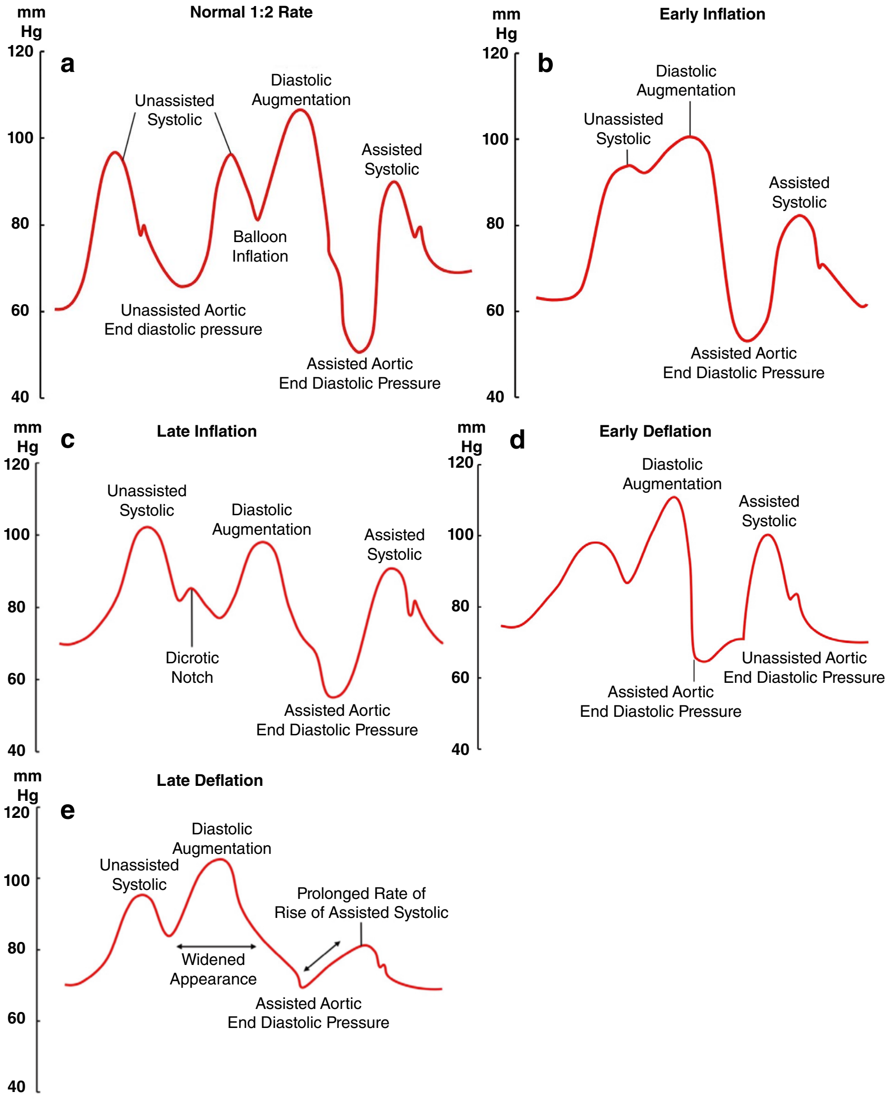

Fig. 52.3 (**a–e**): Normal and suboptimal timing of inflation and deflation. Normal rate of inflation and deflation (**a**); early inflation: inflation of the IAB before aortic valve closure (**b**); late inflation: inflation of the IAB markedly after closure of the aortic valve (**c**); early deflation: premature deflation of the IAB during the diastolic phase (**d**); late deflation: deflation of the IAB after the onset of systole (**e**)

Step 7: Anticipate and Prevent Complications in Relation to IABP

- Trauma to the arterial wall incurred while inserting and advancing the guidewire or balloon (laceration, dissection, subadventitial hematoma) (1–5%)
- Limb ischemia associated with the position of the balloon catheter, which disappears with catheter removal (5–11%)
- Dislodged thrombus created during balloon removal, resulting in distal embolization (peripheral, renal) (1–5%)
- Hematologic (thrombocytopenia, red blood cell hemolysis, hemorrhage) (1–5%)
- Balloon leak/rupture (1–4%)
- Infection (2–4%)
- Cholesterol embolization—presents with fever, thrombocytopenia, livedo reticularis

The likelihood of these complications occurring varies between hospitals. According to the Benchmark Registry, 2.6% of the sample size experienced at least one major complication, such as severe bleeding (0.8%), major limb ischemia (0.9%), or balloon leak (0.05%). Additionally, 7.0% of the sample size experienced either major or minor complications.

Step 8: Identify the Factors Impacting IABP Complications

- *The following factors increase IABP complications:*
  - Peripheral Vascular Disease (PVD)
  - Old age
  - Female sex
  - Diabetes mellitus
  - Hypertension
  - Prolonged support
  - Large catheter size (>9.5 Fr)
  - Low cardiac index
  - Low body surface area (BSA)
  - Sheathed technique

Step 9: Monitoring the Patient While on IABP

- Specialized nursing care with 1:1 nursing every shift is needed to take care of patients.
- The chest X-ray to document position of the catheter tip, which should be at the bifurcation of the left and right main bronchi.
- Three times daily documentation of peripheral pulses.
- Daily measurement of hematocrit, platelet count, and creatinine.

- Anticoagulation parameters.
- Hemodynamic assessment of the patient.

Step 10: Facilitate the Weaning Process Off IABP

- The patient can be weaned if the following criteria are satisfied:
  - Urine output is more than 40 mL/h without the use of diuretics.
  - Improved mentation.
  - Extremities are warm.
  - Hemodynamics appear to be getting better and stable on little or no inotropes.
  - No evidence of ongoing ischemia.

The prognosis for patients with cardiogenic shock or after cardiac arrest remains poor.

Although the use of percutaneous life-support devices such as IABP and VA-ECMO are practical approach followed in medical practice, no survival benefit has been documented.

Despite optimum medical therapy (OMT), the survival outcome of patients in cardiogenic shock is dismal. A new paradigm shift is toward the use of mechanical circulatory support (MCS) devices early enough and not after OMT has failed. By implementing early use of IABP and/or other MCS devices, one mitigates the adverse effects of inotropes/vasopressors such as arrhythmias or limb and organ ischemia. Though the use of IABP has not been profoundly supported by literature, in terms of better survival, it has in the real world shown improved hemodynamics and organ support. Through the combined use of IABP and VA-ECMO in E-CPR and end-stage cardiogenic shock, an era of IABP resurgence has arrived.

Suggested Reading

Li M, Hu L, Li L. Research progress of intra-aortic balloon counterpulsation in the treatment of acute myocardial infarction with cardiogenic shock: a review. Medicine (Baltimore). 2023;102(49):e36500. *Demonstrated significant benefits of preoperative IABP implant, with no vascular problems, compared to intraoperative implant. They also acknowledged two different studies showing improved hemodynamics, success rate of operation, and hospital survival following early application of IABP after emergency PCI intervention in patients with AMI complicated with coronary syndrome*.

Sjauw KD, Engström AE. A systematic review and meta-analysis of intra-aortic balloon pump therapy in ST-elevation myocardial infarction: should we change the guidelines? Eur Heart J. 2009;30(4):459–68.

Somaschini A, Cornara S, Leonardi S, Demarchi A, Fortuni F, Ferlini M, Crimi G, Camporotondo R, Gnecchi M, Oltrona Visconti L, De Servi S, De Ferrari GM. Beneficial effects of IABP in anterior myocardial infarction complicated by cardiogenic shock. Medicina. 2023;59(10):1806. *The loss of benefit of the IABP in the Shock II trial was due to a heterogeneous population, with a large majority experiencing a lower-than-expected incidence of events in the control group.*

They further reported that the use of the IABP in cases of ST-elevation myocardial infarction (STEMI) complicated by cardiogenic shock (CS) improves survival in patients with anterior infarction.

Thiele H, Zeymer U, Neumann FJ, Ferenc M, Olbrich HG, Hausleiter J, Richardt G, Hennersdorf M, Empen K, Fuernau G, Desch S, Eitel I, Hambrecht R, Fuhrmann J, Böhm M, Ebelt H, Schneider S, Schuler G, Werdan K. Intraaortic balloon support for myocardial infarction with cardiogenic shock. New Engl J Med. 2012;367(14):1287–96. *The use of intra-aortic balloon counterpulsation did not have a significant impact on reducing 30-day mortality in patients experiencing cardiogenic shock due to acute myocardial infarction when an early revascularization strategy was planned.*

Appendix A (Tables A.1 and A.2)

Table A.1 Drugs and doses

Drug class/prototypes	Dosing	Common toxicities
ABCD (amphotericin B cholesteryl sulfate complex)	3–4 mg/kg IV q24h	Hypotension, hypokalemia, thrombocytopenia, hypomagnesemia, hepatotoxicity, renal failure allergic reactions
Abacavir	300 mg PO q12h or 600 mg q24h	CNS, skin rash
Abciximab	0.25 mg/kg IV bolus and then 0.125 mcg/kg/min	Hypotension, chest pain, nausea, minor bleeding, back pain
ABLC (amphotericin B lipid complex)	5 mg/kg IV q24h	Hypotension, hypokalemia, thrombocytopenia, hepatotoxicity, renal failure, allergic reactions
Acetaminophen	325–1000 mg PO/IV q4–6h PRN	Rash, anemia, blood dyscrasias, hepatotoxicity
Acetazolamide	250–500 PO/IV mg given q8h	Metabolic acidosis, hypokalemia, hyponatremia, abnormal LFT
Activated charcoal	25–100 g PO	Vomiting, constipation, fecal discoloration (black)
Acetylcysteine	Acetaminophen poisoning Oral: 140 mg/kg followed by 17 doses of 70 mg/kg q4h IV: 150 mg/kg over 60 min f/b 300 mg/kg over 21 h Nebulization: 3–5 mL of 20% solution three to four times a day, administer before chest physiotherapy Prevention of radiocontrast-induced renal injury: 600 mg PO q12h for 3 days starting 1 day before procedure, may be given intravenously	Anaphylactoid reaction, angioedema, vasodilatation, hypotension, tachycardia, urticaria, nausea, vomiting, bronchospasm

(continued)

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Table A.1 (continued)

Drug class/prototypes	Dosing	Common toxicities
Acyclovir	10–15 mg/kg/dose q8h IV (HSV encephalitis) 800 mg PO every 4 h (Herpes Zoster) 400 mg bolus	Reversible renal failure, hepatic toxicity, confusional state
Adenosine	6 mg IV, if not effective in 1–2 min, can give 12 mg, may repeat 12 mg	Flushing, light headedness, headache, nervousness/anxiety
Adrenaline (see epinephrine)		
Albumin	0.5–1 g/kg/dose (5% in hypovolemia)	Hypervolemia, anaphylaxis, chills, fever, tachycardia, bronchospasm
Albuterol	5–10 mg nebulized over 30–60 min	Arrhythmias, chest discomfort, palpitation, CNS stimulation, drowsiness, diarrhea, dry mouth, micturition difficulty
Alfentanil	IV bolus 500 mcg every 10 min as necessary IV infusion: 1 mcg/kg/min	Respiratory depression, apnea, bradycardia, delayed gastric emptying, chest wall rigidity
Allopurinol	600–800 mg/day in two to three divided doses	Rash
Alteplase	15 mg bolus, then 0.75 mg/kg (up to 50 mg) × 30 min, then 0.5 mg/kg (up to 35 mg) × 60 min (maximum 100 mg over 90 min) Pulmonary embolism: 100 mg IV over 2 h Stroke: 0.9 mg/kg 10% bolus, rest over 60 min (Max 90 mg)	Hypotension, bleeding, allergic reactions
Amantadine	100 mg PO q12h	Nausea, vomiting, anorexia, xerostomia
Amikacin	15–20 mg/kg once a day	Ototoxicity, neurotoxicity, nephrotoxicity
Aminophylline	Loading dose; 5 mg/kg IV over 30 min Maintenance: 0.1–0.8 mg/kg/h	Tachycardia, arrhythmia, convulsions
Amiodarone	150–300 mg bolus, then 1 mg/min for 6 h, then 0.5 mg/min for 18 h Oral 200 mg 8 hourly, then titrate down to 200 mg q24h	Bradycardia, hypotension, AV block, nausea, photosensitivity, hypothyroidism, hyperthyroidism, coagulation abnormalities, hepatitis, visual disturbance, pulmonary fibrosis
Amitryptiline	25–75 mg PO q24h	Confusion, dry mouth, retention of urine
Amlodipine	5–10 mg PO q24h	Pedal edema, headache, nausea, vomiting
Amoxicillin/clavulanate	625 mg PO q12h/q8h	Nausea, vomiting, diarrhea, allergic reaction

(continued)

Table A.1 (continued)

Drug class/prototypes	Dosing	Common toxicities
Amphotericin B deoxycholate Amphotericin B (Liposomal)	0.3–1.5 mg/kg IV q24h (diluted in 5% dextrose) 3–5 mg/kg/day (diluted in 5% dextrose)	Hypotension, hypokalemia, thrombocytopenia, hepatotoxicity, creatinine increase, allergic reactions Same as Ampho B, less nephrotoxicity
Ampicillin	250–500 mg IV q4–6h	Fever, allergic reaction, penicillin encephalopathy, diarrhea, pseudomembranous colitis, agranulocytosis, anemia
Ampicillin/sulbactam	IV: 1.5–3 g (1–2 g ampicillin + 0.5–1 g sulbactam) every 8 h	Diarrhea (11–20%), nausea (6–10%), vomiting (4–8%), abdominal pain (3–6%), rash (4–7%), Urticaria (2–5%), pruritus (2–4%), eosinophilia (2–5%)
	for CRAB infections Administer a total daily dose of 9 grams of sulbactam via 1 of the following regimens: 9 grams of ampicillin-sulbactam (6 grams ampicillin, 3 grams sulbactam) IV every 8 h, infused over 4 h	
	OR	
	27 grams of ampicillin-sulbactam (18 grams ampicillin, 9 grams sulbactam) IV as a continuous infusion over 24 h	
Andexanet Alpha (Antidote to rivaroxaban and apixaban)	1.5–3 g IVq6h 400–800 mg bolus @30 mg/min 4–8 mg/min iv infusion for up to 120 min	Fever, allergic reaction, penicillin encephalopathy, diarrhea, pseudomembranous colitis, agranulocytosis, anemia
Anidulafungin	200 mg IV bolus, then 100 mg IV q24h	Elevated LFT
Aqueous penicillin G	2–4 million U IV q4h	Fever, allergic reaction, penicillin Encephalopathy, diarrhea
Argatroban	350 mcg/kg bolus, then 25 mcg/kg/min adjust based on aPTT (For PCI) Initial 2 mcg/kg/min, adjust based on aPTT measurements (for prophylaxis in heparin-induced thrombocytopenia)	Bleeding, cardiac arrest, dyspnea
Arbekacin (aminoglycoside)	150–200 mg once a day i.v.	Nephrotoxicity, ototoxicity
Ascorbic acid	1.5 g over 30 min every 6 h	Oxalate nephropathy
Bromocriptine	2.5–5 mg PO q8h (max. 45 mg for neuroleptic malignant syndrome)	Headache, dizziness, nausea, hypotension, nasal congestion

(continued)

Table A.1 (continued)

Drug class/prototypes	Dosing	Common toxicities
Bumetanide	0.5–2 mg/dose PO q24h	Hyperuricemia, hypochloremia, hypokalemia, azotemia, hyponatremia, hyperglycemia, muscle cramps, creatinine increase
Calcitonin	Initial 4 U/kg IM q12h, up to 8 U/kg IM q6h	Facial flushing, nausea, vomiting
Calcium gluconate/chloride (10 mL of 10%)	1 g IV over 2–5 min	Hypercalcemia, constipation (oral)
Captopril	6.25–50 mg PO q8h	Hypotension, dizziness, abnormal taste, cough, worsening renal function
Carvedilol	6.25 mg PO q12h, maximum 25 mg PO q12h	Hypotension, dizziness, fatigue, hyperglycemia, weight gain, diarrhea, bradycardia, syncope, deranged LFT, bronchospasm
Caspofungin	70 mg IV bolus, then 50 mg IV q24h	Headache, fever, chills, hypokalemia, flushing, tachycardia, anemia, eosinophilia, neutropenia, nephrotoxicity
Cefazolin	1–2 g IV q8h	Allergic reaction, fever, Stevens–Johnson syndrome, nephrotoxicity, diarrhea, nausea, vomiting
Cefepine	*Uncomplicated cystitis*: 1 gram IV every 8 h, infused over 30 min; *All other infections*: 2 grams IV every 8 h, infused over 3 h	Positive coombs test, fever, headache, rash, pruritus, diarrhea, nausea, vomiting, agranulocytosis
Cefiderocol	2 grams IV every 8 h, infused over 3 h CrCL ≥120 mL/min: 2 grams IV every 6 h, infused over 3 h	Infusion site reactions (7.4%), Diarrhea (4.5%) Nausea (3.5%) Vomiting (3.2%) Headache (2.6%) Alanine transaminase (ALT) Increase (2.5%) Aspartate transaminase (AST) Increase (2.4%) Hypokalemia (2.3%) Constipation (2.2%)
Cefoxitin	1–2 g IV q6–8h	Diarrhea, anaphylaxis, nausea, vomiting, headache, rash, pruritus, diarrhea, agranulocytosis, pseudomembranous colitis
Ceftazidime	500 mg IV to 2 g q8–12h	Diarrhea, hypersensitivity reactions, candidiasis, nephrotoxicity, encephalopathy, headache, fever

(continued)

Table A.1 (continued)

Drug class/prototypes	Dosing	Common toxicities
Ceftazidime-avibactam	2.5 g IV every 8 h, infused over 3 h	Hypersensitivity, *C. Difficile*-associated diarrhea, blood dyscrasias, seizures esp. in renal failure patients, constipation, and anxiety (10%)
Ceftazidime-avibactam PLUS aztreonam	*Ceftazidime-avibactam*: 2.5 grams IV every 8 h, infused over 3 h *PLUS* (administered simultaneously via Y-site administration) *Aztreonam***:** 2 grams IV every 8 h, infused over 3 h	Hypersensitivity, *C. Difficile*-associated diarrhea, blood dyscrasias, seizures esp. in renal failure patients, constipation, and anxiety
Ceftolazone Tazobactam	*Uncomplicated cystitis*: 1.5 grams IV every 8 h, infused over 1 h; *All other infections*: 3 grams IV every 8 h, infused over 3 h	Hypersensitivity
Ciprofloxacin	*Uncomplicated cystitis*: 400 milligrams IV every 12 h or 500 milligrams PO every 12 h; *All other infections:* 400 milligrams IV every 8 h *OR* 750 milligrams PO every 12 h	Nausea, diarrhea, abdominal pain, headache, dizziness
Ceftriaxone	1–2 g IV q12–24 h	Headache, rash, pruritus, diarrhea, nausea, vomiting, agranulocytosis
Cefuroxime	0.75–1.5 g IV 6–8 hourly	*C. Difficile* diarrhea Hypersensitivity Transient rise in liver function test
Chlordiazepoxide	10–30 mg PO q8h to q6h	Muscle weakness, ataxia, confusion, hypotension
Cyclosporine	IV: 1–5 mg/kg/day Oral: 1.5 times IV dose q12h	Increased urea, creatinine Hypertension Hirsutism, gingival hypertrophy Hyperuricemia, tremor
Cidofovir	5 mg/kg IV weekly plus probenecid 2 g PO 3 h before the infusion and then 1 g at 2 and 8 h after the infusion	Nephrotoxicity, uveitis/iritis, nausea, vomiting
Ciprofloxacin	500–750 mg PO q12h or 400 mg IV q8–12h	Dizziness, insomnia, restlessness, fever, rash, nausea, vomiting, diarrhea, ALT/AST increase, rhinitis
Clarithromycin	500 mg IV/PO q12h	Headache, nausea, vomiting, diarrhea, abdominal pain, rash

(continued)

Table A.1 (continued)

Drug class/prototypes	Dosing	Common toxicities
Clindamycin	600–1200 mg IV q8h to q6h, maximum 4.8 g/day PO 150–450 mg/dose every 6–8 h, maximum dose 1.8 g/day	Diarrhea, abdominal pain, hypotension, urticaria, rash, pseudomembranous colitis
Clonidine	0.1–0.3 mg PO q12h/8 h	Drowsiness, dizziness, hypotension, bradycardia, dry mouth
Clopidogrel	75 mg PO q24h	Nausea, vomiting, diarrhea, bleeding
Codeine phosphate	30–60 mg PO q4h/q6h	Drowsiness, constipation, respiratory depression
Colistin: Colistimethate sodium (CMS) 1 mg CBA = 30,000 IU CMS 33 mg CBA = 1 MU CMS	IV: Loading dose 300 mg CBA (colistin base activity) (~9 million IU) infused over 0.5–1 h (Body wt/7.5) Administer the first maintenance dose 12–24 h later Maintenance dose: 300–360 mg CBA (~9–10.9 million IU), divided into two and infused over 0.5–1 h at 12-h intervals	Fever, headache, pruritus, rash, GI upset, paresthesia, weakness, apnea, respiratory arrest, renal dysfunction, myopathy
	Nebulization: 2–3 million units q8h	
Conivaptan	20 mg IV bolus, then 0.8–1.6 mg/h IV continuous infusion	Diarrhea, hypokalemia
Co-trimoxazole (trimethoprim: Sulfamethoxazole 1:5)	PCP pneumonia treatment: 15–20 mg/kg/day of trimethoprim IV for 14 days, followed orally for further 7 days	Rash, nausea, vomiting, diarrhea, agranulocytosis, thrombocytopenia, hemolysis in G6PD deficiency, rash, allergic myocarditis, peripheral neuritis, aseptic meningitis, hyperkalemia, interstitial nephritis, Stevens–Johnson syndrome
	PCP prophylaxis: 80 mg trimethoprim orally daily	
Dapagliflozin (SGLT 2 inhibitor)	10 mg OD	Urinary tract infections Increased urination Thirst Hypotension Dizziness Genital mycotic infections (hypoglycemia)
Dalteparin	120 U/kg SC q12h	Bleeding, wound hematoma, pain at injection site, thrombocytopenia, allergic reactions, alopecia

(continued)

Table A.1 (continued)

Drug class/prototypes	Dosing	Common toxicities
Dantrolene	1–2.5 mg/kg IV; may repeat q5–10 min to maximum cumulative dose 10 mg/kg	Drowsiness, dizziness, diarrhea, nausea, vomiting
Daptomycin	4–6 mg/kg IV q24h	Anemia, diarrhea, vomiting, peripheral edema, rash, insomnia, UTI, rise in CPK
DDAVP	0.3 mcg/kg slow IV/SC/IM Intranasally: 5–20 mcg daily	Facial flushing
Deferoxamine	1 g IV bolus, then 500 mg IV q4h × 2 doses	Urine discoloration (orange–red)
Dexamethasone	10 mg IV prior to ACTH stimulation test, 4–6 mg IV q6h/q8h	Same as hydrocortisone
Dexmedetomidine	0.2–0.7 mcg/kg/h IV	Hypotension, bradycardia
Dextran (40)	Maximum 20 mL/kg, 20–40 mL/min IV	Allergic reaction, fluid overload, platelet dysfunction
Diazepam	5–10 mg IV over 2 min	Apnea, respiratory depression, drowsiness, hypotension, bradycardia
Diclofenac	75 mg IM 50 mg PO q8h	
Digoxin	Load: 10–15 mcg/kg; give 50% of load in initial dose, then 25% at 6–12 h Intervals × 2 *Maintenance*: 0.125–0.5 mg/day (dose should be reduced by 20–25% when changing from oral to IV)	Bradycardia, heart block, arrhythmias, yellow vision, rash, muscle weakness
Diltiazem	0.25 mg/kg bolus (may repeat 0.35 mg/kg bolus after 15 min), then 5–15 mg/h (PO (extended release) 60–120 mg q12h)	Bradycardia, hypotension, constipation (verapamil > diltiazem), headache, flushing, edema
Dobutamine	2.5–20 mcg/kg/min	Tachycardia, hypertension, ventricular ectopics, headache, palpitations
Dopamine	5–20 mcg/kg/min	Ectopic beats, tachycardia, arrhythmia, palpitations, angina, headache, dyspnea
Dopexamine	0.25–6 mcg/kg/min	Tachycardia, hypotension, angina, hypokalemia, hyperglycemia
Doxycycline	100 mg PO/IV q12h	Intracranial hypertension, pericarditis, angioneurotic edema, skin hyperpigmentation, bone marrow depression, hepatotoxicity

(continued)

Table A.1 (continued)

Drug class/prototypes	Dosing	Common toxicities
Enalapril	2.5–20 mg PO q12h	Hypotension, dizziness, abnormal taste, cough, worsening renal function
Enoxaparin	1 mg/kg SC q12h	Bleeding, thrombocytopenia
Epinephrine	1 mg IV q3–5 min in cardiac arrest (10 mL of 1 in 10,000 solution) 0.01–0.3 mcg/kg/min IV Infuse via central vein in Shock Anaphylaxis: 0.5–1.0 mL of 1 in 1000 solution (50–100 mcg) may be given subcutaneously Bronchospasm: 0.5–1.0 mL of 1:1000 (0.5–1 mg) diluted with normal saline 2.5 mL and nebulized	Tachycardia, hypertension, angina, arrhythmia, sudden death, dry throat, nausea, vomiting, anxiety, headache, dyspnea, urinary retention
Epoprostenol	2–50 ng/kg/min IV 5000–20,000 ng/mL continuous nebulization	Flushing, headache, nausea vomiting, hypotension, chest pain, palpitation, diarrhea, weight loss, weakness, myalgia
Eptifibatide	180 mcg/kg bolus, then 2 mcg/kg/min	Bleeding, hypotension, thrombocytopenia
Ertapenem	1 g IV q24h	Edema, chest pain, tachycardia, headache, fever, rash, diarrhea, nausea, abdominal pain, hepatic enzyme increase
Erythromycin	250–500 mg PO q6h or 0.5–1 g IV q6h	QTc prolongation, torsades de pointes, pruritus, rash, abdominal pain, anorexia, cholestatic jaundice, neuromuscular weakness, hearing loss
Erythropoietin (recombinant human)	50–300 units/kg weekly in 2–3 divided doses subcutaneously	Hypertension, thrombocytosis, flu-like symptoms, hyperkalemia, shunt, thrombosis
Esmolol	500 mcg/kg bolus, then 50–300 mcg/kg/min	Hypotension, diaphoresis, dizziness, nausea, vomiting
Esomeprazole	20–40 mg PO q24h	Headache, dizziness, pruritus, flatulence, diarrhea
Etomidate	Anesthesia: 0.2–0.6 mg/kg over 30–60 s	Adrenal suppression
Factor VIIa (recombinant)	Hemorrhagic stroke: (Warfarin related) 10–100 mcg/kg IV: Bleeding episode: 90 mcg/kg every 2 h	Hypertension

(continued)

Table A.1 (continued)

Drug class/prototypes	Dosing	Common toxicities
Fentanyl	1–2 mcg/kg/dose Infusion: 1–3 mcg/kg/h	Hypotension, bradycardia, CNS depression, confusion, chest wall rigidity, respiratory depression
Flucloxacillin	1–2 g 6 h	Interstitial nephritis Hemolytic anemia Cholestatic jaundice
Fluconazole	100–800 mg PO/IV q24h	Headache, seizure, rash, angioedema, hypercholesterolemia, hypokalemia, hepatitis, cholestasis
Fondaparinux	2.5 mg SC q24h	Bleeding, fever, nausea, anemia
Flucytosine	25–37.5 mg/kg PO q6h	Nausea, vomiting, diarrhea, rash
Fludrocortisone	50–200 mcg PO q24h	Hypertension, edema, acne, hypokalemic alkalosis, hyperglycemia, peptic ulcer
Flumazenil	0.2–0.5 mg IV q1min, up to 3 mg	Vasodilatation, headache, agitation, dizziness, blurred vision, dyspnea, hyperventilation
Fomepizole	15 mg/kg/IV bolus, then 10 mg/kg IV q12h × 4 doses, then 15 mg/kg IV q12h until ethylene glycol or methanol level <20	Headache, nausea, bradycardia, hypotension, dizziness, metallic taste
Foscarnet	60 mg/kg IV q8h or 90 mg/kg IV q12h	Nephrotoxicity, electrolyte abnormalities (hypocalcemia, hypomagnesemia, hypokalemia, hypophosphatemia), nausea, vomiting, diarrhea, headache
Fosfomycin	Meningitis: 16-24 g/day iv (divided q6-q8h) Bone and joint infection Complicated intraabdominal infection Complicated SSTI Complicated UTI HAP/VAP Infective endocarditis: 12–24g/day iv (q8-12)g/day Uncomplicated UTI 3 g po ×1 dose Complicated UTI 3 g po q2-3 days ×3 doses Prostatitis 3 g po q3 days ×7 doses	Large sodium load (14.4 meq/g), hypokalemia, diarrhea, hematological toxicities, liver injury, headache, taste disturbances

(continued)

Table A.1 (continued)

Drug class/prototypes	Dosing	Common toxicities
Fosphenytoin 75 mg of Fosphenytoin = 50 mg of phenytoin	Loading dose; 15–20 mgPE/kg IV Maintenance; 4–6 mg phenytoin equivalent (PE)/kg/day in two to three divided doses	IV form: Hypotension, bradycardia, phlebitis, nystagmus, rash
Furosemide	20–80 mg/day IV/PO in two to three divided doses	Hypotension, blurred vision, cutaneous vasculitis, gout, hyperglycemia, anorexia, allergic interstitial nephritis, fall in GFR, increased blood urea
Ganciclovir	5 mg/kg IV q12h	Fever, rash, abdominal pain, nausea, vomiting, anemia, leucopenia, thrombocytopenia, confusion, neuropathy, pruritus, paresthesia, retinal detachment
Gemifloxacin	320 mg PO q24h	Headache, dizziness, rash
Gentamicin	3 mg/kg bolus, then 2 mg/kg IV q8h or 5–7 mg/kg extended interval (q24h to q12h or divided dose)	Vertigo, ataxia, gait instability, ototoxicity, nephrotoxicity, edema, pruritus
Glutamine	5 g 6 hourly orally 0.3–0.4 g/kg body weight IV	Increase in AST and ALT
Haloperidol	0.5–5 mg 2–3 times/day/max 30 mg IV/PO 2–10 mg IV bolus, repeat bolus every 15–30 min with sequential doubling of dose	CNS depression, orthostatic hypotension, arrhythmia, alopecia, extrapyramidal symptoms, neuroleptic malignant syndrome, cholestatic jaundice
Heparin	Prophylaxis: 5000 units 8–12 hourly Therapeutic: 60 units/kg bolus f/b 12 units/kg/h infusion maximum 1000 units/h	Bleeding, hyperkalemia, cutaneous necrosis, elevated liver enzymes, peripheral neuropathy
Hydralazine	10–40 mg IV q4–6h or 10–75 mg PO q8h/q6h	Hypotension, tachycardia, flushing, headache
Hydrocortisone	Septic shock: 200–300 mg/day in three to four divided doses or as continuous infusion	Hyperglycemia, mood changes, insomnia, gastrointestinal irritation, increased appetite, GI bleed, hypokalemia Long-term: Osteoporosis, acne, fat redistribution, muscle wasting, cataracts, increased blood pressure, infection

(continued)

Table A.1 (continued)

Drug class/prototypes	Dosing	Common toxicities
Hypertonic saline (23.4% NaCl)	For mannitol refractory patients: 3–50 mL q3–6h as needed (central line only), 0.686 mL of 23.4% saline is equimolar to 1 g of mannitol	Hypernatremia, hyperchloremia, fluid overload, pulmonary edema
Ibuprofen	200–800 mg PO q3–6h	Edema, dizziness, itching, fluid retention, dyspepsia, tinnitus, hypocalcemia
Ilioprost	2.5–5 mcg inhaled six to nine times daily	Flushing, hypotension, headache, nausea, trismus, cough, flu-like syndrome, jaw pain, syncope, hemoptysis
Imipenem + cilastatin	*Uncomplicated cystitis*: 500 mg IV every 6 h, infused over 30 min *All other infections*: 500 mg IV every 6 h, infused over 3 h	Tachycardia, seizure, oliguria, nausea, diarrhea
Imipenem-cilastatin-relebactam	1.25 grams IV every 6 h, infused over 30 min	Tachycardia, seizure, oliguria, nausea, diarrhea
Ipratropium	2–4 puffs (15 mcg/actuation) q12h to q6hNebulised: 500 mcg 3–4 times/day	Bronchitis, upper respiratory tract infection, palpitation, dizziness, rash, nausea
Isavuconazole	IV: Initial 200 mg 8 hourly for six doses Maintenance: 200 mg once daily	Peripheral edema, QT shortening
Isoprenaline	Up to 20 mcg/min IV infusion, titrate according to heart rate	Tachycardia, arrhythmia, angina, hypotension
Isosorbide dinitrate	5–40 mg PO q8h	Hypotension, headache, dizziness, flushing
Isosorbide mononitrate (extended release)	30–120 mg PO q24h	Hypotension, headache, dizziness, flushing
Itraconazole Kayexalate	200 mg IV/PO q24h Oral: 15 g 1–4 times daily Rectal: 30–50 g every 6 h	Pruritus, nausea, vomiting, chills Ischemic colitis Bezoar
Ketorolac Ketamine	15–30 mg IV q6h 20 mg PO f/b 10 mg q6–8h intubation: 1–2 mg/kg iv over 1–2 min	Headache, abdominal pain, dyspepsia, nausea, edema, drowsiness, diarrhea tachycardia Hypertension Delirium
Labetalol	100–400 mg PO q8–12h (max 2.4 g/day) 20–40 mg IV (maximum 80 mg) as bolus at 10–20 min intervals (max. 300 mg), then 0.5–2 mg/min infusion if needed	Dizziness, hypotension, bradycardia, nausea, vomiting, transaminase increase, paresthesia, flushing, headache

(continued)

Table A.1 (continued)

Drug class/prototypes	Dosing	Common toxicities
Lactulose	20–30 g (30–45 mL) PO q2h until initial stool, then adjust to maintain two to three soft stools/day	Diarrhea, flatulence, nausea
Lacosamide	Status epilepticus: 200–600 mg IV daily	CNS
Lansoprazole	30–60 mg PO q12–24 h	Headache, abdominal pain, nausea, diarrhea
Lepirudin	0.5 mg/kg IV loading over 5 min as a loading dose (0.2 mg in renal failure) 0.15 mg/kg/h continuous IV infusion adjust based on aPPT measurements	Bleeding
Levalbuterol	Adjust based on aPPT measurements 0.63–0.125 mg q8h 2–4 puff TID (45 mcg/actuation)	Hyperglycemia, hypokalemia, tremors, rhinitis, viral infection, headache, migraine, rash, abdominal cramps
Levetiracetam	500–1000 mg IV/PO q12h	Behavior changes, somnolence, nausea, vomiting, anorexia, weakness, cough, facial edema, bruising
Levofloxacin	750 milligrams IV/PO every 24 h	Chest, pain, edema, nausea, vomiting, dyspnea, pharyngitis, rash, CNS stimulation, seizure, dizziness, somnolence
Levosimendan	Loading dose (may be omitted) 6–12 mcg/kg given over 10 min 0.1 mcg/kg/min continuous infusion	Hypotension, tachycardia, headache, nausea, dyspnea
Levothyroxine	50–100 mcg IV Q6–8h × 24 h, then 100 mcg IV q24h	Angina, arrhythmia, MI, palpitations, tachycardia, anxiety, headache, hyperactivity, insomnia, alopecia, tremors
Lidocaine	1–1.5 mg/kg IV bolus (may repeat doses 0.5–0.75 mg/kg in 5–10 min up to maximum 3 mg/kg), then 1–4 mg/min	Arrhythmia, bradycardia, heart block, hypotension, edema, flushing, anxiety, hallucinations, seizures
Linezolid	600 mg IV/PO q12h	Headache, diarrhea, insomnia, rash, nausea, constipation, thrombocytopenia, anemia, leucopenia, abnormal liver tests
Liothyronine	200–500 mcg (in myxedema coma)	Tachycardia, arrhythmia
Lisinopril	2.5–40 mg PO q24h	Hypotension, dizziness, abnormal taste, cough, worsening renal function

(continued)

Table A.1 (continued)

Drug class/prototypes	Dosing	Common toxicities
Lorazepam	Status epilepticus: 4 mg IV bolus, 0.5–4 mg/h Sedation: 0.02–0.06 mg/kg bolus Infusion: 0.01–0.1 mg/kg/h	Sedation, hypotension, confusion, dermatitis, rash
Magnesium sulfate	4–6 g IV over 15–20 min, then 2 g/h infusion (1 g of mg So$_4$ = 98.6 mg of elemental mg = 8.12 meq of elemental magnesium)	Hypermagnesemia, diarrhea (oral)
Mannitol (10–20%)	1–1.5 g/kg IV bolus, then 0.25–1 g/kg q3–6h as needed	Hypotension, acute renal failure, fluid and electrolyte imbalances
Meropenem	*Uncomplicated cystitis*: 1 gram IV every 8 h, infused over 30 min *All other infections*: 2 grams IV every 8 h, infused over 3 h	Headache, rash, diarrhea, anemia, phlebitis, agranulocytosis, TEN, glossitis
Meropenem-vaborbactam	4 grams IV every 8 h, infused over 3 h	Headache, rash, diarrhea, anemia, phlebitis, agranulocytosis, TEN, glossitis
Methimazole	Initial 30–60 mg/day in three divided doses q8h, maintenance 5–30 mg/day PO	Vasculitis, CNS stimulation, alopecia, agranulocytosis
Methylprednisolone	Pulse therapy: 15–30 mg/kg/day for 3 days IV Spinal cord injury: 30 mg/kg over 15 min IV f/b 5.4 mg/kg/h for 23 h (unlabeled use)	Hypertension, arrhythmia, insomnia, seizure, psychosis, hirsutism, adrenal suppression, diabetes mellitus, hypokalemia, hyperglycemia, peptic ulcer, pancreatitis, osteoporosis, muscle weakness
Metoclopramide	10 mg PO/IV q8h to q6h	Bradycardia, AV block, CHF, drowsiness, dystonic reaction, rash, agranulocytosis, bronchospasm
Metoprolol	IV: 5 mg every 2 min for three doses f/b 50 mg orally q6h for 48 h, then 100 mg q12h	Bradycardia, hypotension, syncopy, Raynaud's disease, dizziness, fatigue, bronchospasm, diarrhea, rash
Metronidazole	500 mg IV/PO q8h	Nausea, vomiting, metallic taste, disulfiram-like reaction
Micafungin	50–150 mg IV q24h	Headache, hypokalemia, hypocalcemia, leucopenia, neutropenia, transaminase increase, rigors
Midazolam	1–5 mg bolus, 1–10 mg/h, 0.2 mg/kg bolus, then 0.75–10 mcg/kg/min	Sedation, hypotension, confusion, dermatitis, rash
Milrinone	50 mcg/kg/bolus, then 0.25–0.75 mcg/kg/min	Hypotension, arrhythmia

(continued)

Table A.1 (continued)

Drug class/prototypes	Dosing	Common toxicities
Minocycline	200 milligrams IV/PO every 12 h	Vestibular symptom (30–90%), vertigo, ataxia, nausea vomiting, skin pigmentation, hypersensitivity pneumonitis, fever rash, photosensitivity, eosinophilia
Morphine sulfate	2.5 mg IV q3–4h Infusion: 1–10 mg/h	Constipation, dyspepsia, nausea, drowsiness, dizziness
Moxifloxacin	400 mg IV/PO q24h	
Naloxone	0.4–2 mg IV q2min, up to 10 mg	Narcotic withdrawal
Neomycin	500–2000 mg PO q6–12h	Nausea, vomiting, diarrhea, irritation, or soreness of mouth or rectal area
Neostigmine	2.5 mg IV bolus, may be repeated in 3 h	Sweating, salivation, abdominal cramps, diarrhea, bradycardia
Nesiritide	2 mcg/kg bolus, then 0.01–0.03 mcg/kg/min	Hypotension, increased serum creatinine, arrhythmia
Nicardipine	3–15 mg/h IV infusion PO: 20 mg q8h	Hypotension, tachycardia, headache, flushing, peripheral edema
Nifedipine (immediate release) extended release	30 mg once daily PO up to 30 mg q8h 30–120 mg PO q24h	Hypotension, tachycardia, headache, flushing, peripheral edema
Nimodipine	60 mg q6h to q4h orally in subarachnoid hemorrhage	Hypotension
	1–2 mg/h in hypertensive emergencies.	Elevated liver enzyme
Nitric oxide	5–40 ppm inhalation	Hypotension, flushing, rashes, withdrawal syndrome
Nitroglycerin	10–200 mcg/min IV infusion	Nausea, vomiting, headache, hypotension, tachycardia, thiocyanate, and cyanide toxicity
Nitrofurantoin	Macrocrystal/monohydrate: 100 mg PO every 12 h Oral suspension: 50 milligrams PO every 6 h	Nausea, vomiting, diarrhea, abdominal pain, hepatotoxicity, rashes pruritis
Nitroprusside	Usual, 0.25–3 mcg/kg/min, maximum 10 mcg/kg/min	Nausea, vomiting, hypotension, tachycardia, thiocyanate and cyanide toxicity
Norepinephrine	0.02–3 mcg/kg/min IV infusion	Hyperglycemia, bradycardia, skin necrosis, arrhythmia
Octreotide	25–50 mcg IV bolus, then 25–50 mcg/h infusion 50–100 mcg SC q8h	Diarrhea, flatulence, nausea, abdominal cramps, bradycardia, dysglycemia
Ofloxacin	200–400 mg PO q12h	Chest pain, headache, rash, diarrhea, visual disturbance, pharyngitis
Olanzapine	2.5–5 mg daily	Drowsiness

(continued)

Table A.1 (continued)

Drug class/prototypes	Dosing	Common toxicities
Omeprazole	20–40 mg PO/IV q12–24 h/IV infusion 8 mg/h	Headache, dizziness, rash, vomiting, taste perversion
Ondansetron	8–10 mg PO/q24h/q12h	Headache, malaise, drowsiness, fever, pruritus, diarrhea
Oseltamivir	Prophylaxis: 75 mg PO q24h Treatment: 75 mg PO q12h	Vomiting, nausea, abdominal pain, allergy, anaphylaxis
Oxacillin	2 g IV q4–5h	Headache, rash, diarrhea, anemia, phlebitis, agranulocytosis, TEN, glossitis
Pamidronate	60–90 mg IV	Renal failure, allergic reaction, hypotension
Pancuronium	50–100 mcg/kg IV bolus f/b 1–2 mcg/kg/min IV infusion	Tachycardia, hypertension
Pantoprazole	20–40 mg PO q12–24 h, 80 mg IV bolus, then 8 mg/h × 72 h	Chest pain, headache, rash, diarrhea, visual disturbance, pharyngitis
Paracetamol	IV: 1 g every 4–6 hourly Oral: 0.5–1 g 6 hourly	Hypotension Hepatotoxicity
Pentamidine	Treatment PCP: 4 mg/kg IV q24h for 14–21 days; prophylaxis PCP: 300 mg/dose monthly inhalation	Renal failure, leucopenia, thrombocytopenia, pancreatitis, hypoglycemia
Phenobarbital	20 mg/kg IV bolus	Sedation, nystagmus, ataxia, nausea, vomiting IV form: Hypotension, bradycardia, respiratory depression
Phentolamine	2–5 mg IV bolus 0.1–2 mg/min IV infusion	Hypotension, tachycardia, dizziness
Phenylephrine	0.5–10 mcg/kg/min	Arrhythmia, hypertension, chest pain
Phenytoin	20 mg/kg IV bolus, then 5–6 mg/kg/day PO/IV	Concentration-dependent: Nystagmus, diplopia, ataxia, sedation, lethargy, mood/behavior changes, coma, seizures
Phosphate salts (over 6 h IV infusion)	0.08–0.16 mmol/kg	Hyperphosphatemia
Plazomicin	*Uncomplicated cystitis*: 15 mg/kg IV as a single dose *Pyelonephritis or complicated urinary tract infections*: 15 mg/kg IV OD	Nephrotoxicity, ototoxicity, hypersensitivity.
Piperacillin/tazobactam	3.375–4.5 g IV q6h	Diarrhea, hypertension, insomnia, rash, transaminase increase, moniliasis, fever
Polymyxin B	Loading dose: 25000 IU/kg over 2 h Maintenance dose: 15,000–25,000 IU/kg/day in two divided doses	Neurotoxicity, nephrotoxicity, neuromuscular blockade, respiratory arrest

(continued)

Table A.1 (continued)

Drug class/prototypes	Dosing	Common toxicities
Posaconazole	For prophylaxis of Aspergillus and Candida IV/Delayed release tablets: 300 mg bd, 2 doses, then 300 mg OD. Oral suspension: 200 mg q8h	Nausea, vomiting, abdominal pain, headache, diarrhea, nephrotoxicity, adrenal insufficiency, QTc prolongation.
Potassium chloride	Daily requirement: 40–80 mEq/day	Rash, hyperkalemia, thrombophlebitis, abdominal pain, constipation (oral)
	Deficiency correction: 10 mEq/h infusion, maximum 40 mEq/h for first 3–4 h	
Potassium iodide	50–100 mg 1–2 drops or 0.05–0.1 mL PO q8–12h	Metallic taste, nausea, stomach upset, diarrhea, salivary gland swelling
Procainamide	15–18 mg/kg bolus, then 1–4 mg/min infusion	Hypotension, rash, diarrhea, nausea, vomiting
Propofol	Bolus: 0.5–3 mg/kg over 3–5 min f/b 5–50 mcg/kg/min infusion	Hypotension, bradycardia, arrhythmia, CNS depression, apnea, hypertriglyceridemia, thrombophlebitis
Propranolol	40 mg PO q12h, maximum 640 mg/day	AV conduction disturbance, cardiogenic shock, Raynaud's syndrome, psychosis, alopecia, anorexia, impotence, agranulocytosis
Propylthiouracil	Initial 300 mg PO in three divided doses q8h, maintenance 50–300 mg/day	Vasculitis, CNS stimulation, alopecia, agranulocytosis
Prostacyclins Epoprostenol	1–20 ng/kg/min	Jaw pain, nausea, headache, flushing, hypotension, infusion-site pain
Protamine	10 mg IV is required to neutralize 1000 units of unfractionated heparin in previous 15 min	Hypersensitivity, hypotension
Pyridostigmine	60–240 mg PO q4h to q6h	Sweating, salivation, abdominal cramps
Quinupristin/dalfopristin	7.5 mg/kg IV q12hr	Hyperbilirubinemia, arthralgia, myalgia
Quetiapine	12.5–200 mg 12 hourly	Dizziness, dry mouth, sedation
Ramipril	1.25–5 mg PO q12h	Hypotension, dizziness, abnormal taste, cough, worsening renal function
Ranitidine	50 mg IV q8h	Hypersensitivity, bradycardia, thrombocytopenia, leucopenia reversible, transient rise in LFT
Rasburicase	0.2 mg/kg IV q24h × 5 days	Nausea, vomiting, fever, headache, rash, diarrhea, constipation

(continued)

Table A.1 (continued)

Drug class/prototypes	Dosing	Common toxicities
Remifentanil	0.5–1 mcg/kg/min (induction of anesthesia)	Hypomagnesemia, bradycardia, hypotension
Reteplase	10 mg IV, then 10 mg IV 30 min after the first dose	Hypotension, bleeding, allergic reactions
Rezafungin	Loading dose: 400 mg IV on Day 1 Maintenance dose: 200 mg IV once weekly	Nausea (14%) Vomiting (12%) Diarrhea (11%) Abdominal pain (10%) Headache (10%) Infusion site reactions (10%)
Rifampicin	10 mg/kg/day PO q24h, maximum 600 mg/day	Edema, flushing, ataxia, pemphigoid reaction, adrenal insufficiency, agranulocytosis, hepatitis, myalgias, acute renal failure
Rocuronium	Intubation: 0.6–1.2 mg/kg Maintenance: 0.01–0.012 mg/kg/min infusion	Hypotension/hypertension, arrhythmia, acute quadriparetic myopathy, bronchospasm
Rifaximin	400 mg PO q8h	Headache
Sacubitril/valsartan (ARNI)	HF: 97/103 mg twice daily (sacubitril/valsartan) Hypertension: 49/51 mg to 97/103 mg twice daily	Hypotension (18%) Dizziness (11%) Hyperkalemia (9%) Cough (6%) Diarrhea (5%) Fatigue (5%) Headache (5%)
Salbutamol	Nebulized: 2.5–5 mg 4–6 hourly	Tachycardia
Sildenafil	20 mg PO q8h (pulmonary hypertension)	Headache, dyspepsia, flushing, dizziness, diarrhea, anemia, leucopenia, abnormal vision
Sucralfate	1 g suspension 4 hourly	Constipation
Sulbactam-durlobactam	Sulbactam 1 gram/durlobactam 1 gram (2 grams total) IV every 6 h, infused over 3 h CrCL ≥130 mL/min**:** Sulbactam 1 gram/durlobactam 1 gram (2 grams total) IV every 4 h, infused over 3 h	Diarrhea (6.8%), nausea (4.5%), vomiting (3.4%), headache (3.2%), pyrexia (2.9%), infusion site reactions (2.6%), abdominal pain (2.4%), constipation (2.2%), rash (2.1%), pruritus
Suxamethonium	1.0–1.5 mg/kg IV bolus; rapid sequence intubation	Hyperpyrexia, muscle pain, hyperkalemia
Teicoplanin	400 mg 12 hourly for three doses IV, then 400 mg q24h IV	Raised LFT, hypersensitivity, thrombocytopenia

(continued)

Table A.1 (continued)

Drug class/prototypes	Dosing	Common toxicities
Telmisartan (angiotensin II receptors blocker)	Hypertension: 20–80 mg once daily Heart failure: 20–40 mg twice daily	Dizziness (7%) Headache (6%) Fatigue (5%) Diarrhea (5%) Upper respiratory tract infections (5%) Back pain (4%) Cough (4%) Hypotension
Tenecteplase	One-time bolus over 5 s: ≤60 kg = 30 mg 61–70 kg = 35 mg 71–80 kg = 40 mg 81–90 kg = 45 mg ≥90 kg = 50 mg	Hypotension, bleeding, allergic reactions
Terlipressin	Hepatorenal syndrome: 0.5–1 mg q6h IV Varices: 2 mg IV bolus, then 1–2 mg q4–6h IV	Hypertension, abdominal cramps
Theophylline	Bolus: 5 mg/kg if no theophylline received in the previous 24 h Maintenance: 0.7 mg/kg/h	Arrhythmia, headache, seizure, nervousness, nausea, diarrhea, tremor, muscle cramp
Thiopental	2.5–4 mg/kg IV bolus for seizure control	Apnea, bronchospasm, hypersensitivity
Thiourea drugs	Initial 300–600 mg q24h PO	Rash, arthralgias, fever, leucopenia, nausea, vomiting
Ticarcillin/clavulanate	3.1 g IV q4–6h	Diarrhea, hypertension, insomnia, rash, transaminase increase, moniliasis, fever
Tigecycline	200 mg IV as a single dose, then 100 mg IV every 12 h	Nausea, hypertension, peripheral edema, phlebitis, fever, headache, insomnia, pruritus, hyperglycemia, hyperproteinemia, hyperkalemia, thrombocytopenia, leukocytosis, hepatic dysfunction, neuromuscular weakness
Tobramycin	Uncomplicated cystitis: 5 mg/kg and the AST profile of the pathogen, IV as a single dose pyelonephritis or complicated urinary tract infections: 7 mg/kg IV OD	Nephrotoxicity, ototoxicity, hypersensitivity

(continued)

Table A.1 (continued)

Drug class/prototypes	Dosing	Common toxicities
Tirofiban	0.4 mcg/kg/min × 30 min, then 0.1 mcg/kg/min (in unstable angina), 0.4 mcg/kg/min × 3 min, then 0.1 mcg/kg/min (in PCI)	Bleeding, bradycardia, coronary artery dissection, dizziness, vasovagal reaction, thrombocytopenia
Torsemide	10–20 mg IV/PO daily Maximum: 200 mg (PO, IV)	Arrhythmia, chest pain, headache, ototoxicity, dizziness, hyperglycemia, hyperuricemia, hypokalemia
Tranexamic acid	500–1000 mg 8 hourly	Thrombosis
Trimethoprim-sulfamethoxazole	*Uncomplicated cystitis*: 160 mg (trimethoprim component) IV/PO every 12 h	Nephrotoxicity, ototoxicity, hypersensitivity
Valproate	1000–2500 mg/day IV/PO q12h to q6h maintenance loading (in status epilepticus): 15–45 mg/kg IV at <6 mg/kg/min infusion (in status epilepticus): 1–4 mg/kg/h	Somnolence, diplopia, nausea, vomiting, diarrhea
Vancomycin	Loading (in severe infection): 25–30 mg/kg f/b 15–20 mg/kg IV q8–12h 125–500 mg PO in *C. difficile* diarrhea	Bitter taste, nausea, vomiting, chills, fever, eosinophilia, interstitial nephritis, vasculitis, thrombocytopenia, red man syndrome
Vasopressin	40 units IV bolus 0.01–0.04 U/min IV Infusion (in refractory septic shock) 0.2–0.4 U/min IV infusion (in variceal hemorrhage)	Arrhythmia, asystole, decreased cardiac output, chest pain, MI, peripheral ischemia, venous thrombosis, urticaria, mesenteric ischemia
Verapamil	5–10 mg iv bolus	Bradycardia
Vericiguat	Initial dose: 10 mg once daily Maintenance dose: 10–15 mg once daily	Hypotension (22%) Dizziness (10%) Headache (8%) Nausea (6%) Diarrhea (5%) Fatigue (5%) Increased creatinine (5%)
Vecuronium	100 mcg/kg iv	Liver dysfunction
Vitamin K	1–10 mg PO, SQ, or IV q24h	Hemolysis in G6PD deficiency
Voriconazole	i.v. 6 mg/kg for two doses q12h, first day f/b 4 mg/kg IV q12h Oral maintenance: 200 mg 12 hourly	Photophobia, agranulocytosis, thrombocytopenia, anemia, diarrhea, vomiting, hallucinations, tachycardia, hyper−/hypotension, raised liver enzymes, cholestatic jaundice
Warfarin	Initial 1–5 mg PO q24h, adjust based on INR measurements	Bleeding, angina, chest pain, hypotension, alopecia, skin necrosis, agranulocytosis, purple toe syndrome

Table A.2 Dosage modification in renal failure

Medication	Dose for normal renal function	Dose with impaired renal function (GFR mL/min/1.73 m^2)			Supplemental dose in dialysis	
		30–50	10–29	<10	Hemodialysis (HD)	Peritoneal dialysis (PD)
Antimicrobials						
Acyclovir	PO: 80 mg/kg/day, divided q6h IV: 30 mg/kg/day	10 mg/kg, q12h	10 mg/kg, q24h	5 mg/kg, q24h	Yes CVVHD/CVVHDF: 10 mg/kg q12–24 h	No
Amikacin	5–7.5 mg/kg/dose, q8–12h or 15–20 mg/kg IV OD	5–7.5 mg/kg, q12–18 h	5–7.5 mg/kg, q24h	5–7.5 mg/kg, q48–72 h	Yes CVVHD/DF: Loading dose 10 mg/kg f/b maintenance 7.5 mg/kg q24–48 h	Yes
Amphotericin B (conventional)	0.5–1.5 mg/kg IV, q24h	No change	No change	No change	No	No
Ampicillin	100–200 mg/kg/day, divided q6h	No change	Usual dose q6–12h	Usual dose q12–24 h	Yes CVVHD/DF: Loading dose 2 g followed by 1–2 g q6–8h	No
Amoxicillin	20–50 mg/kg/day IV/PO, divided q8h	No change	10–20 mg/kg/dose, q12h	10–20 mg/kg/dose, q24h	Yes	No
Azathioprine	1–3 mg/kg, q24h PO	Reduce dose by 25%	Reduce dose by 25%	Reduce dose by 50%	Yes	Yes
Azithromycin	10 mg/kg/day PO/IV	No change	No change	No change	No	No
Caspofungin	70 mg on day 1, then 50 mg IV, q24h	No change	No change	No change	No	No
Co-amoxiclav	IV/PO: 10–20 mg/kg, q8h	No change	Increase interval, q12h	Increase interval, q24h	Yes	No
Cefaclor	20–40 mg/kg/day IV, divided q8–12h	No change	No change	Reduce dose by 50%; divided q12h	Yes	No
Cefepime	50 mg/kg/dose IV, q12h	50 mg/kg/dose, q24h	50 mg/kg/dose, q24h	50 mg/kg/dose, q48h	Yes CVVHD/DF: Loading dose 2 g f/b 2 g q12h	No

Cefixime	8–10 mg/kg/day, divided q12h PO	No change	Reduce daily dose by 25%	Reduce daily dose by 50%	Yes	No
Cefotaxime	100–200 mg/kg/day IV, divided 6–8 h	50 mg/kg/dose q8–12h	50 mg/kg/dose, q12h	50 mg/kg/dose, q24h	Yes CVVHD/DF: 1–2 g q6–8h	No
Ceftazidime	100–150 mg/kg/day IV, divided 8 h	50 mg/kg/dose, q12h	50 mg/kg/dose, q24h	50 mg/kg/dose, q48–72 h	Yes CVVHD/DF: Loading dose 2 g f/b 2gm q12h	Yes
Ceftazidime avibactam	2.5 g 8 hourly	1.25 g 8 hourly	0.94 g every 12 h	0.94 every 24 h	Administer post dialysis	
Ceftriaxone	75–100 mg/kg/day IV, divided q12–24 h	No change	No change	No change	No	No
Cefuroxime	PO: 20–30 mg/kg/day, divided q12h IV: 50–100 mg/kg/day, divided q8h	No change	50 mg/kg/dose, q12h	50 mg/kg/dose, q24h	Yes CRRT 1 g q12h	No
Cephalexin	30–50 mg/kg/day PO, divided q6h	5–10 mg/kg/dose, q8h	5–10 mg/kg/dose, q12h	5–10 mg/kg/dose, q24h	Yes	No
Cefoperazone	100 mg/kg/day IV, divided 12 h	No change	No change	No change	Yes	No
Cefoperazone/sulbactam	30–60 mg/kg/day (total), 10–20 mg/kg/day of sulbactam IV	No change	50% dose of sulbactam	25% dose of sulbactam	Yes	No

(continued)

Table A.2 (continued)

Medication	Dose for normal renal function	Dose with impaired renal function (GFR mL/min/1.73 m^2)			Supplemental dose in dialysis	
		30–50	10–29	<10	Hemodialysis (HD)	Peritoneal dialysis (PD)
Ciprofloxacin Colistin	PO: 20 mg/kg/day, divided q12h IV: 10 mg/kg/day, divided q12h 9–10.9 million loading Maintenance nine million unit daily divided into two doses 300–360 mg CBA loading 300 mg CBA daily divided in two doses	No change 5.9–6.65 million units/day (195–220 mg CBA/day)	q12–24 h 4.85–5.9 million units/days (160–195 mg CBA/day)	q24h 4.4 million/day (145 mg CBA/day)	Yes CVVHD/DF: 200–400 mg q12–24 h *intermittent hemodialysis* (IHD): On a nondialysis day (~3.95 million IU/day). 130 mg CBA/day on a dialysis day, administer a supplemental dose (~1.2 million IU) 40 mg CBA–(~1.6 million IU) 50 mg CBA for a 3- or 4-h IHD session, respectively *Sustained low-efficiency dialysis* (SLED) that 10% of the CMS dose be added to the baseline daily dose per 1 h of SLED CRRT (~13.3 million IU/day) 440 mg CBA/day = (~6.65 million IU every 12 h). 220 mg CBA every 12 h	Yes

Co-trimoxazole	6–10 mg/kg/day (TMP), IV/PO divided q12h	No change	5–10 mg/kg/dose, q12h	Not recommended	Yes	No
Daptomycin	6 mg/kg/dose IV, q24h	No change	4 PO/IV/kg/dose, q24h	4 mg/kg/dose, q48h	No CVVHD: 8 mg/kg q48h	No
Erythromycin	30–50 mg/kg/day IV/PO, q6–8h	No change	No change	50% dose	No	No
Fluconazole	6–12 mg/kg IV/PO, q24h	Reduce dose by 50%	Reduce dose by 50%	Reduce dose by 50%	Yes CVVHD/DF loading dose: 400–800 mg f/b 400–800 mg q24h	No
Gentamicin	2–2.5 mg/kg IV, q8h	q12h	q18–24 h	q24–48 h	Yes CVVHD/DF 1.5–2.5 mg/kg q24–48 h (9 redose when concentration <3–5 mg/L)	Yes
Imipenem Cilastatin	60–100 mg/kg/day IV, divided q6h; maximum daily dose 4 g	20 mg/kg, q8h	10 mg/kg, q12h	10 mg/kg, q12h	Yes CRRT: Loading dose 1 g f/b 500 mg q6h	No
Itraconazole	3–10 mg/kg/day PO, q24h	No change	No change	No change	No	No
Linezolid	10 mg/kg/dose PO/IV, q8h	No change	No change	No change	Yes	Yes
Lamivudine	4 mg/kg, q12h PO	4 mg/kg, q24h	2 mg/kg, q24h	1 mg/kg, q24h	Yes	No
Metronidazole	20–25 mg/kg/day IV/PO, divided q8h	No change	No change	Reduce daily dose by 50%	No	No
Meropenem	60–120 mg/kg/day IV, divided q8h	20–40 mg/kg, q12h	10–20 mg/kg, q12h	10–20 mg/kg, q24h	Yes CRRT: Loading dose of 1 g f/b 1 g q8–12h	10–20 mg/kg q24h

(continued)

Table A.2 (continued)

Medication	Dose for normal renal function	Dose with impaired renal function (GFR mL/min/1.73 m^2)			Supplemental dose in dialysis	
		30–50	10–29	<10	Hemodialysis (HD)	Peritoneal dialysis (PD)
Netilmicin	4–7.5 mg/kg IV, divided q8–12h	2 mg/kg, q12h	2 mg/kg, q12h	2 mg/kg, q24–48 h	Yes	Yes
Ofloxacin	15 mg/kg/day IV/PO, q12h	7.5 mg/kg/dose, q24h	7.5 mg/kg/dose, q24h	7.5 mg/kg/dose, q48h	Yes	No
Penicillin G	50,000–200,000 U/kg/day IV, divided q4–6h	No change	Reduce daily dose by 25%, divided q8–12h	Reduce daily dose by 50%, divided q12–16 h	Yes	No
Piperacillin/tazobactam	150–300 mg/kg/day IV, divided q6–8h	Reduce dose by 30%, q6h	Reduce dose by 30%, q8h	Reduce dose by 30%, q8h	Yes CRRT: 2.25–3.375 g q6h	No
Teicoplanin	10 mg/kg IV, q12h for 3 doses IV, then 10 mg/kg IV, q24h	Normal loading dose, then 1–4 mg/kg, q24h	Normal loading dose, then 1–4 mg/kg, q24h	Normal loading dose, then 1 mg/kg, q24h	No	No
Tobramycin	2.5 mg/kg/dose, q8h	q12h	q24h	q48h	Yes	Yes
Valganciclovir	450 mg/m^2/day or 30 mg/kg/day q24h	50%	25%	25%		Yes
Vancomycin	10–15 mg/kg IV, q6–8h	10 mg/kg, q12h	10 mg/kg, q24h	10 mg/kg, q48–72 h	No	No
Voriconazole	6 mg/kg/dose IV/PO, q12h on day 1, then 4 mg/kg, q12h	No change	No change	No change		Yes
Miscellaneous						
Allopurinol	10 mg/kg/dose PO, q24h	Reduce dose by 50%	Reduce dose by 50%	Reduce dose by 75%	Yes	Yes
Amlodipine	0.05–0.15 mg/kg/day PO	No change	No change	No change	No	No

Aspirin	1–5 mg/kg/day PO	No change	No change	Avoid	Yes	Yes
Atenolol	1–3 mg/kg PO, q24h	Normal dose	50% dose, q24h	50% dose, q48h	Yes	No
Cyclosporine	3–6 mg/kg/day	No change	No change	No change	No	No
Digoxin	6–10 μg/kg/day	75% dose	50% dose	25% dose	No	No
Enalapril	0.1–1 mg/kg/day	75% dose	75% dose	50% dose	Yes	No
Enoxaparin	1 mg/kg/day, q12–24 h	No change	70% dose	50% dose, q24h	No	No
Furosemide	1–6 mg/kg/day divided PO 6–12 h	No change	No change	No change	No	No
Heparin	50–200 U bolus f/b 20 U/kg/h	No change	No change	50% dose	No	No
Hydrochlorothiazide	2 mg/kg/day, q12h	No change	Avoid	Avoid	Avoid	Avoid
Labetalol	5–20 mg/kg/day, q12h PO	No change	No change	No change	No	No
Metoclopramide	0.2–0.8 mg/kg/day, divided q6–8h	Reduce dose by 25%	Reduce dose by 50%	Reduce dose by 75%	Yes	No
Mycophenolate mofetil	600–1200 mg/m^2/day	No change	No change	No change	No	No
Nitroprusside	0.3–8 μg/kg/min	No change	No change	No change	Yes	Yes
Prazosin	50–500 μg/kg/day	No change	No change	75% dose	No	No
Propanolol	0.5–4 mg/kg/day divided q6–8h	No change	No change	No change	No	No
Ramipril	6 mg/m^2, q24h	No change	50% dose	25% dose	No	NA
Ranitidine	PO: 3–6 mg/kg/day, divided q12h IV: 2–4 mg/kg/day, divided q8h	Reduce dose by 25%	Reduce dose by 25%	Reduce dose by 50%	No	No
Tacrolimus	0.15 mg/kg/day	No change	No change	No change	No	No
Warfarin	0.1–0.3 mg/kg/day	No change	No change	No change	No	No

(continued)

Table A.2 (continued)

Medication	Dose for normal renal function	Dose with impaired renal function (GFR mL/min/1.73 m^2)			Supplemental dose in dialysis	
		30–50	10–29	<10	Hemodialysis (HD)	Peritoneal dialysis (PD)
Antitubercular drugs						
Ethambutol	15–25 mg/kg, q24h	No change	Increase interval, q36h	Increase interval, q48h	Yes	No
Isoniazid	10–15 mg/kg/day, q12–24 h	No change	No change	No change	Yes	Yes
Pyrazinamide	30 mg/kg, q24h	No change	50% dose	Normal dose after HD, 3 weeks	Yes	Yes
Rifampicin	10–20 mg/kg/day, q12–24 h	No change	No change	No change	No	No
Streptomycin	20–40 mg/kg, q12–24 h IM	q24–72 h	q24–72 h	q24–72 h	Yes	Yes
Anticonvulsants						
Carbamazepine	10–30 mg/kg/day, divided 8 h	No change	No change	No change	No	No
Clonazepam	0.05–0.5 mg/kg/day	No change	No change	75% dose	No	No
Lamotrigine	2 mg/kg/day in two single doses for 2 weeks, then 5 mg/kg for 2 weeks, then 5–15 mg/kg/day	No change	No change	75% dose	No	No
Levetiracetam	10–60 mg/kg/day, divided 8 h	50% dose	50% dose	50% dose	Yes	Yes
Phenobarbitone	5–8 mg/kg/day	No change	No change	50% dose	Yes	Yes
Phenytoin	5–8 mg/kg/day	No change	No change	No change	No	No
Topiramate	3–9 mg/kg/day, divided 8–12 h	50% dose	50% dose	25% dose	Yes	NA
Valproate sodium	10–60 mg/kg/day	No change	No change	No change	No	No

Appendix B

Common ICU Formulae

A. *Pulmonary equations*

1. *Arterial oxygen tension (PaO_2)*
   On room air = 100 − 1/3 (age)
   On supplemental oxygen = FiO_2 (in decimals) × 500, Room air FiO_2 = 21% (0.21), FiO_2 increases by approximately 4% for each liter increase in supplemental oxygen
2. *Alveolar gas equation*

$$PAO_2 = \left(FiO_2 \times \left[Patm - PH_2O\right]\right) - \left(\frac{PaCO_2}{R}\right)$$

$$PAO_2 = 150 - \left(1.25 \times PaCO_2\right)$$

   Normal = 100 mmHg (room air, at sea level).
   where PAO_2 = alveolar partial pressure of oxygen.
   FiO_2 = fraction of inspired oxygen (in decimals).
   Patm = barometric pressure (760 mmHg at sea level).
   PH_2O = water vapor pressure (47 mmHg at normal body temperature 37 °C).
   $PaCO_2$ = partial pressure of carbon dioxide in the blood.
   R = respiratory quotient, assumed to be 0.8.
3. *Alveolar–arterial oxygen gradient $PAO_2 - PaO_2$*
   - A-a gradient (on room air) = 2.5 + 0.21 × age in years
   - Normal value = 3–15 mmHg
     Varies with FiO_2
   - For FiO_2 = 21%; A-a gradient = 5–15 mmHg
   - For FiO_2 = 100%; A-a gradient = <150 mmHg
4. *PaO_2/FiO_2 ratio* Normal = 300–500 mmHg
   <300 = acute lung injury (previous definition).
   <200 = ARDS (previous definition) Berlin definition:

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- 200–300 (with PEEP/CPAP >5) = Mild ARDS
- <200 (with PEEP >5) = Moderate ARDS
- <100 (With PEEP >5) = Severe ARDS.

5. *Arteriolar–alveolar oxygen ratio* = PaO_2/PAO_2 Normal = 0.77–0.82 (most reliable when $FiO_2 < 0.5$)
6. Oxygenation index =

$$\left[\text{mean air way pressure } \left(\text{cm } H_2O\right) \times \frac{FiO_{2(\text{fraction of inspired } O_2)}}{PaO_{22(\text{mm Hg})}}\right] \times 100,$$

0—25 = Good outcome
>25–40 = severe hypoxemia

7. *Static lung compliance (Crs)*

$$\text{Compliance}_{\text{static}} = \frac{\text{Tidal volume}}{\text{Plateau pressure} - \text{PEEP}\begin{pmatrix}\text{positive end}\\ -\text{ expiratory pressure}\end{pmatrix}}$$

Normal compliance in an intubated patient = 57–85 mL/cm H_2O

8. *Dynamic lung compliance (Crs dynamic)*

$$\text{Compliance}_{\text{dynamic}} = \frac{\text{Tidal volume}}{\text{Peek pressure} - \text{PEEP}\begin{pmatrix}\text{positive end}\\ -\text{ expiratory pressure}\end{pmatrix}}$$

Variable depending on peak pressure in an intubated patient
Lung + Thoracic wall compliance = 0.1 L (100 mL)/cm H_2O (Crs)

9. *Airway resistance*

$$\text{Airway resistance} = \frac{\text{Peak inspiratory pressure} - \text{plateau pressure}}{\text{Peak inspiratory flow}}$$

Normal resistance in an intubated patient is 4–6 cm H_2O/L/s

10. *$PaCO_2$–$PetCO_2$ gradient* Normal = 4–5 mmHg
11. *Dead space ventilation* $\frac{V_D}{V_T} = \frac{PaCO_2 - PetCO_2}{PaCO_2}$

V_D = Dead Space Ventilation = 1 mL/lb (2.2 kg) of ideal body wt = 150 mL V_T = Tidal Volume

$$\frac{PetCO_2 = \text{end} - \text{tidal } CO_2 \text{ measured by capnography}}{\text{Normal } V_D / V_T = 0.5(50\%) \text{ in mechanically ventilated patients } (30\%)}$$

in spontaneously breathing patients

12. *Shunt equation (right to left shunt)* $Qs / Qt = \frac{(CcO_2 - CaO_2)}{(CcO_2 - CvO_2)}$

- Qs/Qt = shunt fraction
- CcO_2 is the end-capillary oxygen content (estimated from the PAO_2)
- CaO_2 is the arterial oxygen content
- CvO_2 is the mixed venous oxygen content
- Normal = 5%

Alternate equation (in patients breathing 100% oxygen for 20 min)

$$Qs / Qt = 100 \times \left(0.0031 \times AaG\right) / \left(\left(.0031 \times AaG\right) + 5\right)$$

13. *$PaO_2 + PaCO_2 < 150$ mmHg at sea level breathing room air*
14. *ROX index: (Respiratory oxygenation index): (SpO2/FiO2)/Respiratory rate*

    Assessed as a predictor of the need to intubate the patients who received HFNC oxygen therapy.

    Interpretation:

    - *ROX Index ≥4.88: Low risk of mechanical ventilation*
    - *ROX Index 2.85–4.87: Moderate risk of mechanical ventilation*
    - *ROX Index ≤2.84: High risk of mechanical ventilation*
15. *HACOR SCORE: Clinical score to predict NIV failure among patients with hypoxemic acute respiratory failure based on following 5 components:*

Variable	Value	Score
HR	≤120	0
	≥121	1
pH	≥7.35	0
	7.30–7.34	2
	7.25–7.29	3
	<7.25	4
Glasgow	15	0
	13–14	2
	11–12	5
	≤10	10
PaO_2/Fi_2	>201	0
	176–200	2
	151–175	3
	126–150	4
	101–125	5
	≤100	6
RR	≤30	0
	31–35	1
	36–40	2
	41–45	3
	≥46	4

A HACOR score >5 at 1 h of NIV highlights patients with a >80% risk of NIV failure regardless of diagnosis, age, and disease severity

16. SBI (rapid shallow breathing index): also known as the Tobin Index, which predicts weaning success from mechanical ventilation, this identifies patients at risk for respiratory failure, monitors disease progression in chronic respiratory conditions (e.g., COPD), and guides respiratory therapy and ventilation strategies.

$$\text{RSBI} = \text{Respiratory Rate}\left(\text{RR}\right) / \text{Tidal Volume}\left(\text{VT}\right)$$

Interpretation:
Low RSBI: <100: Indicates adequate respiratory function
High RSBI: ≥100: Suggests respiratory distress, potential need for mechanical

17. TRANSPULMONARY PRESSURE (TPP):

$$\text{TPP} = \text{Airway pressure}\left(\text{Paw}\right) - \text{Pleural pressure}\left(\text{Ppl}\right).$$

Normal Values:
Rest: 5–10 cm H_2O
Maximal inspiration: 20–30 cm H_2O
Abnormal Values:
Elevated TPP: >30 cm H_2O (indicative of lung stiffness or respiratory muscle weakness).
Decreased TPP: <5 cm H_2O (suggestive of lung collapse or atelectasis).

18. DRIVING PRESSURE (ΔP) = Pplat—PEEP = Change in Volume (ΔV)/Lung Compliance (Crs)

$$\text{Recommended}\,\Delta P < 15\,\text{cmH2O}$$

19. MECHANICAL POWER: The energy transferred from the ventilator to the lungs, measured in Watts (W) or Joules per minute (J/min).

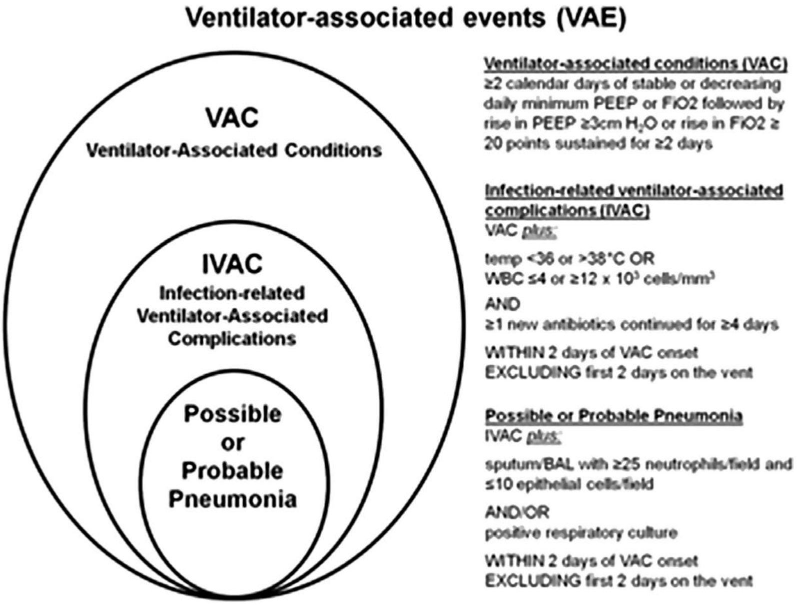
Year	*First author*	*Calculation*	*Note*
2016	Cressoni M	$\text{Power}_{\text{rs}} = \text{RR} \cdot \int_{\text{EELV}}^{\text{EELV}+\text{V}_\text{T}} \text{f}\left(\text{V}\right)\text{dV}$ f(V) = airway pressure at given volume	Known as the “gold standard” method for both controlled and assisted ventilation modes
2016	Gattinoni L	$\text{Power}_{\text{rs}} = \text{RR} \cdot \left\{ V_\text{T}^2 \cdot \left[\frac{1}{2} \times \text{EL}_{\text{rs}} + \text{RR} \times \frac{1+I:E}{60 \cdot I:E} \cdot R_{\text{aw}} \right] + V_\text{T} \cdot \text{PEEP} \right\}$ $\text{Power}_{\text{rs}} = 0.0989 \times V_\text{T} \times \text{RR} \times (P_{\text{peak}} - 1/2 \times \Delta P)$	Applicable for volume-controlled mode with constant inspiratory flow
2016	Guerin C	$\text{Power}_{\text{rs}} = 0.098 \times V_\text{T} \times \text{RR} \times \Delta P$	Simple but considers only the driving pressure-related power

(continued)

Year	*First author*	*Calculation*	*Note*
2019	Becher T	$\text{Power}_{rs} = 0.098 \times V_T \times \text{RR} \times (\Delta P + \text{PEEP})$	Applicable for pressure-controlled mode Overestimates but has good consistency with the actual power
2019	Giosa L	$\text{Power}_{rs} = \dfrac{V_T \cdot RR \times \left(P_{\text{peak}} + \text{PEEP} + \text{F}/6\right)}{30}$	Another simple equation to estimate mechanical power without any intervention volume-

- Healthy lungs: 1–5 J/min
- Mechanical ventilation: <17 J/min recommended

20. Ventilator-Associated Events (VAEs): Complications that occur in patients who are mechanically ventilated.


Ventilator-associated events (VAE)
VAC
Ventilator-Associated Conditions
IVAC
Infection-related
Ventilator-Associated
Complications
Possible
or
Probable
Pneumonia

Ventilator-associated conditions (VAC)
≥2 calendar days of stable or decreasing daily minimum PEEP or FiO2 followed by rise in PEEP ≥3cm H_2O or rise in FiO2 ≥ 20 points sustained for ≥2 days

Infection-related ventilator-associated complications (IVAC)
VAC *plus:*

temp <36 or >38°C OR
WBC ≤4 or ≥12 x 10^3 cells/mm^3

AND
≥1 new antibiotics continued for ≥4 days

WITHIN 2 days of VAC onset
EXCLUDING first 2 days on the vent

Possible or Probable Pneumonia
IVAC *plus:*

sputum/BAL with ≥25 neutrophils/field and ≤10 epithelial cells/field

AND/OR
positive respiratory culture

WITHIN 2 days of VAC onset
EXCLUDING first 2 days on the vent

21. Light's criteria

Light's criteria for pleural effusions		
	Transudate	Caudate
Protein (pleural/serum)	≤0.5	>0.5
LOH (pleural/serum)	≤0.6	>0.6
	Pleural LDH ≤ two-thirds upper limit of normal serum LDH	Pleural LDH > two-triads upper limit of normal scrum LOH

(continued)

Light's criteria for pleural effusions		
	Transudate	Caudate
Common causes	Hypoalbuminemia (cirrhosis, nephrotic syndrome) Congestive heart failure Constrictive pericarditis	Autoimmune disease Esophageal rupture Infection (parapneumonic, TB, fungal, empyema) Malignancy Pancreatitis Post-CABG PE

Ventilatory ratio is defined as [minute ventilation (ml/min) × Pa_{CO2} (mm Hg)]/(predicted body weight × 100 × 37.5).
Normal Value 1
An elevated value of VR would represent either increased pulmonary dead space, increased. VCO_2 or both.

22. S/F ratio
23. $SpO_2/FiO_2 = 0.80\ (PaO_2/FiO_2) + 60$ can be used to predict the S/F ratio from the P/F ratio.
S/F ratios correlate with P/F ratios. S/F ratios of 235 and 315 correlate with P/F ratios of 200 and 300, respectively, for diagnosing and following up patients with ALI and ARDS.

B. *Hemodynamic equations*
(see Chap. 16, Vol. 1)

Parameter	Formula	Normal range
Pulse pressure variation (PPV)	(SVmax − SVmin)/[(SVmax + SVmin)/2] × 100	<10% unlikely to be preload responsive >13–15% likely to be preload responsive
Stroke volume variation (SVV)	SV × (MAP − PAWP) × 0.0136	<10% unlikely to be preload responsive >13–15% likely to be preload responsive
Left ventricular stroke	SVI × (MAP − PAWP) × 0.0136	58–104 g m/beat
Work (LVSW)		
Left ventricular stroke work index (LVSWI)	SV × (MPAP − RAP) × 0.0136	50–62 g m/m^2/beat
Right ventricular stroke work (RVSW)	SVI × (MPAP − RAP) × 0.0136	8–16 g m/beat
Right ventricular stroke work index (RVSWI)	Diastolic BP − PAWP	5–10 g m/m^2/beat
Coronary artery perfusion pressure (CPP)		60–80 mmHg

CVP central venous pressure, *MPAP* mean pulmonary artery pressure, *HR* heart rate, *BP* blood pressure, *PAOP* pulmonary artery occlusion pressure, SaO_2 arterial oxygen saturation, SvO_2 mixed venous oxygen saturation, PaO_2 arterial oxygen partial pressure, PvO_2, mixed venous oxygen partial pressure

- *Cardiac index (CI)*: Greater than 3.0 L/min/m^2
- *Global end diastolic volume (GEDI)*: 700–800 mL/m^2
- *Intravascular blood volume index (ITBI)*: 850–1000 mL/m^2
- *Stroke volume variation (SVV)*: Less than 10%
- *Extravascular lung water (ELWI)*: 3–7 mL/kg
- *Central venous oxygen saturation ($ScvO_2$)*: 70–80%

C. *Acid–base equations*

1. *Validity of the data* Henderson's equation

$$\frac{H^+ \times HCO_3}{PaCO_2} = 24$$

   - H^+ = hydrogen ion
   - HCO_3 = Bicarbonate
   - $PaCO_2$ = Partial pressure of carbon dioxide

pH	$[H^+]$ (mmol/L)
7.60	25
7.55	28
7.50	32
7.45	35
7.40	40
7.35	45
7.30	50
7.25	56
7.20	63
7.15	71

Rule of thumb: H^+ = 80 minus the last two digits of pH after decimal (for pH 7.20–7.50)
For example, pH 7.35: H^+ = 80–35 = 45

2. *Respiratory acidosis or respiratory alkalosis*
   - Acute respiratory acidosis or alkalosis: DpH = 0.008 × $DPaCO_2$ (from 40)
   - Chronic respiratory acidosis or alkalosis: DpH = 0.003 × $DPaCO_2$ (from 40)
   - Acute respiratory acidosis = ↑$PaCO_2$ 10 mmHg = ↑HCO_3 1 mmol/L
   - Chronic respiratory acidosis = ↑$PaCO_2$ 10 mmHg = ↑HCO_3 3 mmol/L
   - Acute respiratory alkalosis = ↓$PaCO_2$ 10 mmHg = ↓HCO_3 2 mmol/L
   - Chronic respiratory alkalosis = ↓$PaCO_2$ 10 mmHg = ↓HCO_3 4 mmol/L
   - Acute respiratory acidosis or alkalosis: SBE (standard base excess) = zero
   - Chronic respiratory acidosis or alkalosis: Change in bicarbonate = 0.4 × SBE
3. *Metabolic acidosis*
   - Predicted $PaCO_2 = 1.\ 5 \times [HCO_3^- + 8] \pm 2$
   - Change in bicarbonate = change in standard base excess (SBE)
   - 1 mEq/L fall in HCO_3 = 1.2 mmHg fall in $PaCO_2$
   - Bicarbonate deficit (mEq/L) = $[0.5 \times \text{body weight (kg)} \times (24 - [HCO_3-])]$
     Rule of thumb: Expected $PaCO_2$ = the last two digits of pH after decimal

4. *Metabolic alkalosis*
   - Predicted $PaCO_2 = 0.7 \times [HCO_3 + 21] \pm 2$
   - Change in bicarbonate = 0.6 × standard base excess (SBE)
   - 1 mEq/L rise in HCO_3 = 0.7 mmHg rise in $PaCO_2$
   - Bicarbonate excess $[0.4 \times \text{body weight (kg)} \times ([HCO_3^-] - 24)]$

     Rule of thumb: Expected $PaCO_2$ = the last two digits of pH after decimal.
5. *Blood anion gap*
   - Anion gap (AG) = $Na^+ - (C^- + HCO_3^-)$
   - Normal value: 10 ± 4 mmol/L
   - Correction for albumin: For every change (increased or decreased) of 1 g/dL in albumin, a change of 2.5 mmol/L in the anion gap
   - Correction for pH: In acidosis, decrease by 2 mmol/L; in alkalosis, increase by 2 mmol/L
6. *Delta gap/Delta ratio*
   - Delta gap = *delta* AG − *delta* $\mathbf{HCO_3^-}$
   - Delta ratio = delta AG/delta HCO_3
   - Where *Delta* AG = patient's AG—12 mEq/L {normal AG}
   - *Delta* HCO_3^- = 24 mEq/L {normal HCO_3^-} − patient's HCO
   - Normal delta gap (in pure anion gap metabolic acidosis) = 0 ± 6
   - Normal delta ratio = 1.1.
   - High delta gap/delta ratio > 1 signifies a concomitant metabolic alkalosis or chronic respiratory acidosis.
   - Low delta gap/delta ratio < 1 signifies a concomitant normal anion gap metabolic acidosis or chronic respiratory alkalosis.
7. *Urine anion gap (UAG)*
   - UAG (mmol/L) = urine [(Na + K) − Cl]
   - Normal: usually zero or positive
   - Nonanion gap metabolic acidosis due to gastrointestinal loss: UAG negative
   - Nonanion gap metabolic acidosis due to renal cause (renal tubular acidosis): UAG positive
8. *Stewarts approach*
   - Strong ion difference (SID): $[Na^+] + [K^+] + [Ca^{2+}] + [Mg^{2+}] - [Cl^-] - [\text{lactate}]$
   - Normal value: 40 mEq/L (Na-Cl) > 40 = alkaosis, <40 = acidosis
   - Increase in SID = alkalosis (increase in pH)
   - Decrease in SID = acidosis (decrease in pH)
   - Strong ion gap (SIG): $SID - SID_{eff}$
   - SID_{eff} = effective strong ion difference (depends on pH, albumin, phosphate).
   - $12.2 \times PCO_2/(10 - pH) + [\text{albumin}] \times (0.123 \times pH - 0.631) + [PO4-] \times (0.309 \times pH - 0.469)$

- Normal SIG = 0
- Positive SIG = Increase in organic acid

D. *Electrolyte equations*

1. *Hyponatremia*
   - Sodium deficit = (desired [Na+] − current [Na+]) × 0.6 × body weight in kg
   - Increase in serum sodium = (infusate sodium − serum sodium)/[(0.6 × body weight) + 1]
   - *Rule of thumb*:
     - For hypertonic (3%) saline, infusion rate (mL/h) = weight (kg) × desired rate of correction (mEq/h)
     - e.g., to correct sodium by 0.5 meq/l/h, the desired rate of 3% saline infusion in a 60 kg man would be = 60 × 0.5 = 30 mL/h
     - 0.9% NaCl corrects at 1–2 mmol/L for every 1 L NaCl
   - Calculated urine osmolarity = the last two digits of urine-specific gravity × 30
2. *Hypernatremia*

$$\text{Free water deficit}\left(\text{L}\right) = 0.4 \times \text{body weight} \times \left(\frac{\text{plasma Na}^{+}}{140} - 1\right)$$

3. *Correction sodium for hyperglycemia*
   - For each 100 mg/dL, blood glucose increases above 200 mg/dL and serum sodium decreases by 2.4 mEq/L.
4. *Serum osmolality*
   - Calculated Sosm = (2 × serum [Na]) + [glucose, in mg/dL]/18 + [blood urea nitrogen, in mg/dL]/2.8
   - Calculated Sosm with standard units (mmol/L) = (2 × serum [Na]) + [glucose] + [urea]
     - Normal value = 270 and 290 mOsm/kg H_2O
   - Osmolar gap = measured osmolality − calculated osmolality
     - Normal value = <10 mOsm/kg H_2O
5. *Corrected calcium*
   - Corrected calcium (mg/dL) = measured total calcium (mg/dL) + [0.8 × (4.0 − albumin)]
   - Corrected calcium (mmol/L) = measured total calcium (mmol/L) + [0.02 × (Normal albumin [40 g/L]—patients albumin)]

E. *Renal equations*

1. *Measured creatinine clearance (CCr) L/day*
   - [24-h urine creatinine (mg/dL) × 24-h urine volume (L/day)]/serum creatinine (mg/dL)
   - CCr mL/min = [(CCr L/day × 1000 mL/L)]/1440 min/day
   - CCr mL/min × 1.73/BSA = CCr mL/min/1.73 sq. m
     - Normal values = 95 ± 20 mL/min per 1.73 m^2 in women and 120 ± 25 mL/min per 1.73 m^2 in men

2. *Estimated creatinine clearance (Cockroft–Gault equation)*
    - (140-age in years × weight in kg)/serum creatinine in mg/dL × 72. For female patients, multiply with 0.85
3. *Fractional excretion of sodium (FENa+)*

$$\frac{\left[\text{UrineNa}^{+}\right]\times\left[\text{plasma creatinine}\right]}{\left[\text{Urine creatinine}\right]\left[\text{plasmaNa}^{+}\right]}$$

    - Normal value = <1
4. *Fractional excretion of urea (FEurea)*

$$\frac{\left[\text{Urineurea}\right]\times\left[\text{plasma creatinine}\right]}{\left[\text{BUN}\right]\times\left[\text{urine creatinine}\right]}$$

    - <35 in prerenal azotemia, 50–65 in acute tubular necrosis

F. *Nutrition equations*

1. *Ideal or predicted body weight (IBW)*
    - Male IBW (kg) = 50 + (0.91 × (height in cm − 152.4))
    - Male IBW (kg) = 50 kg for 5 ft.; add 2.3 kg for every 1 in. above 5 ft
    - Female IBW (kg) = 45.5 + (0.91 × (height in cm − 152.4))
    - Female IBW (kg) = 45.5 kg for 5 ft.; add 2.3 kg for every 1 in. above 5 ft
2. *Harris–Benedict equation with Long's modification (calories requirement)*
    - For women, basal metabolic rate (BMR) = 65.5 + (9.6 × weight in kg) + (1.8 × height in cm) − (4.7 × age in years)
    - For men, BMR = 66 + (13.7 × weight in kg) + (5 × height in cm) − (6.8 × age in years)
    - Actual energy needs = BMR × AF × IF (AF, activity factor; IF, injury factor)
    - Activity factor (AF): Confined to bed = 1.2; out of bed = 1.3
    - Injury factor (IF): Minor surgery = 1.2; skeletal trauma = 1.3; major sepsis = 1.6; severe burn = 2.1
    - Normal calories requirement = 25–30 kcal/kg of predicted body weight
3. *Protein requirement*
    - 1 g of nitrogen = 6.25 g of protein
    - Non-protein calories (NPC)–nitrogen ratio = 150:1
    - Nitrogen balance = (protein intake/6.25) − (24-h urinary urea nitrogen +4)
    - Negative nitrogen balance >5 = severe stress
    - 1 g of nitrogen loss = 30 g lean body mass lost
    - 1 g of glucose = 4 kcal
    - 1 g of protein = 4 kcal
    - 1 g of lipid = 9 kcal
    - Protein loss in dialysis = 4–6 g/h in hemodialysis; 40–60 g in peritoneal dialysis
4. *Respiratory quotient (RQ):*
    - Carbon dioxide production (VCO_2)/oxygen consumption (VO_2)
    - Normal value on balanced diet = 0.7–1.0

  - >1: Excess carbohydrate
  - <0.7: Excess fat

G. *Intra-abdominal pressure equation*

- Abdominal perfusion pressure (APP) = mean arterial pressure (MAP) − IAP (intra-abdominal pressure)
- Normal intra-abdominal pressure = 5–7 mmHg
- Filtration gradient (FG) = glomerular filtration pressure (GFP) − proximal tubular pressure (PTP) = MAP −2 × IAP

H. *Statistical equations*

- Sensitivity: True positives/(true positive [TP] + false negative [FN])
- Specificity: True negative/(true negative [TN] + false positive [FP])
- Positive predictive value: True positive/(true positive + false positive)
- Negative predictive value: True negative/(true negative + false negative)
- Positive likelihood ratio (LR+): sensitivity/(1 − specificity)
- Negative likelihood ratio (LR −): (1 − sensitivity)/specificity
- Prevalence (pretest probability): (TP + FN)/(TP + FP + TN + FN)
- Pretest odds: Prevalence/(1 − prevalence)
- Posttest odds: Pretest odds × LR
- Posttest probability: Posttest odds/(posttest odds +1)
- Event rate (ER): Total events/total subjects (event + nonevent)
- Absolute risk reduction (ARR): Control event rate (CER) − experimental event rate (EER)
- Relative risk reduction (RRR): (CER − EER)/CER
- Relative risk (RR): EER/CER
- Odds ratio: (experimental event [EE]/experimental nonevent [EN])/(control event [CE]/control nonevent [CN])
- Number needed to treat (NNT): 1/ARR
- Number needed to harm (NNH): 1/(CER − EER)
- Rate of type I error = Number of false positives = Alpha
- Rate of type II error = Number of false negatives = Beta
- Power of a test = (1-Beta)

I. *Neurology equations*

- CBF = (CAP − JVP) ÷ CVR
  (CBF, cerebral blood flow; CAP, carotid artery pressure; JVP, jugular venous pressure; CVR, cerebrovascular resistance)
- CPP = MAP − ICP
  (CPP, cerebral perfusion pressure; MAP, mean arterial pressure; ICP, intracranial pressure)
  - Keep CPP between 60 and 75 mmHg
- Increased WBC in traumatic tap:
  Rule of thumb: Subtract one WBC for every 500–1500 RBCs (if peripheral WBC is normal)

J. *Hematology equation*

- DIC SCORE: (ISTH)

Scoring System for DIC		
Parameter	Result	Score
Platelet count	>100 K	0
	<100 K	1
	<50 K	2
D-dinner	<1mcg/ml	0
	1.0-5.0 mcg/ml	2
	> 5.0 mcg/ml	3
PTT	<3 sec	0
	>3 sec	1
	>6 sec	2
Fibrinogen	>100 mg/dl	0
	<100 mg/dl	1

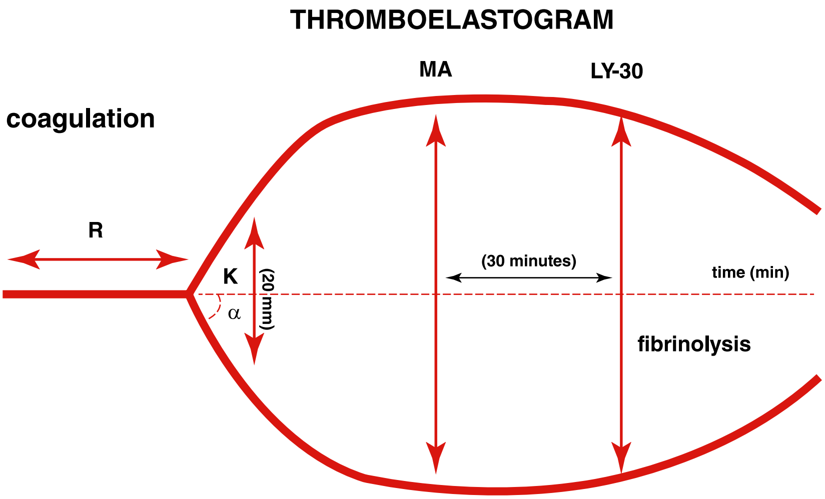
Score ≥5 is indicative of overt DIC with increasing scores correlating with higher mortality.

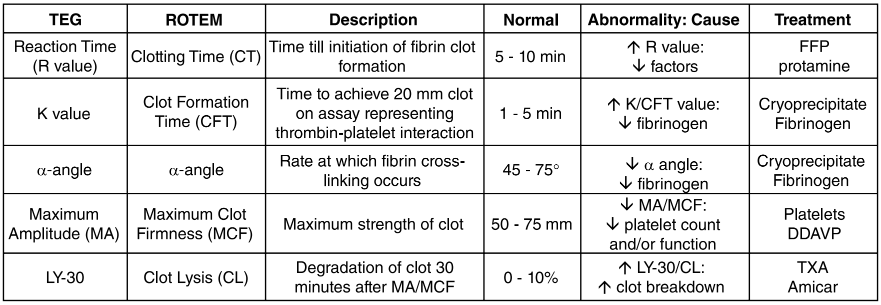
- 4 T SCORE

4Ts Category	2 Points	1 Point	0 Point
Thrombocytopenia	Platelet count fall >50% and platelet nadir ≥20	Platelet count fall 30–50% or platelet nadir 10–19	Platelet count fall platelet nadir <
Timing of platelet count fall	Clear onset days 5–10 or platelet count fall ≤1 day (prior heparin exposure within 30 days)	Consistent with days 5–10 fall, but not clear (e.g., missing platelet counts); order after day 10; or fall ≤1 day (prior heparin exposure 30–100 days ago)	Platelet count fall without recent
Thrombosis or other sequels	New thrombosis (confirmed); skin necrosis; acute systemic reactions postintravenous unfractionated heparin bolus	Progressive or recurrent thrombosis; nonnecrotizing (erythematous) skin lesions; suspected thrombosis (not proven)	None
Other causes of thrombocytopenia	None apparent	Possible	Definite

Abbreviation: *HIT* heparin-induced thrombocytopenia
−3 = Low probability
4–5 = Moderate probability
6–8 = High probability

- THROMBOELSTOGRAPH (TEG):





TEG	ROTEM	Description	Normal	Abnormality: Cause	Treatment
Reaction Time (R value)	Clotting Time (CT)	Time till initiation of fibrin clot formation	5 - 10 min	↑ R value: ↓ factors	FFP protamine
K value	Clot Formation Time (CFT)	Time to achieve 20 mm clot on assay representing thrombin-platelet interaction	1 - 5 min	↑ K/CFT value: ↓ fibrinogen	Cryoprecipitate Fibrinogen
α-angle	α-angle	Rate at which fibrin cross-linking occurs	45 - 75°	↓ α angle: ↓ fibrinogen	Cryoprecipitate Fibrinogen
Maximum Amplitude (MA)	Maximum Clot Firmness (MCF)	Maximum strength of clot	50 - 75 mm	↓ MA/MCF: ↓ platelet count and/or function	Platelets DDAVP
LY-30	Clot Lysis (CL)	Degradation of clot 30 minutes after MA/MCF	0 - 10%	↑ LY-30/CL: ↑ clot breakdown	TXA Amicar

- ANC = WBC × [(segs/100) + (bands/100)]
  (ANC, absolute neutrophil count)

TEG	ROTEM	Description	Normal	Abnormality: Cause	Treatment
Reaction time (R value)	Clotting time (CT)	Time till initiation of fibrin clot formation	5–10 min	↑ R value: ↓ factor	FFP Protamine
K value	Clot formation time (CFT)	Time to achieve 20 mm clot on assay representing thrombin-platelet interaction	1–5 min	↑ K/CFT value: ↓ fibrinogen	Cryoprecipitate Fibrinogen
α-Angle	α-Angle	Rate at which fibrin cross-linking occurs	45–75°	↓ α angle: ↓ fibrinogen	Cryoprecipitate Fibrinogen

(continued)

TEG	ROTEM	Description	Normal	Abnormality: Cause	Treatment
Maximum amplitude (MA)	Maximum clot firmness (MCF)	Maximum strength of clot	50–75 mm	↓ MA/MCF ↓ platelet count and/or function	Platelets DDAVP
LY-30	Clot lysis (CL)	Degradation of clot 30 min after MA/MCF	0–10%	↑ LY-30/CL: ↑ clot breakdown	TXA Amicar

$$\text{Corrected reticulocyte count}\left(\text{CRC}\right)=\frac{\text{reticulocytes}\left(\%\right)}{0.45\text{L}/\text{L}}\times\text{Hct}\left(\text{L}/\text{L}\right)$$

K. Pulmonary Score

- CURB 65: Confusion (1 point), Urea >20 (2 points), Respiratory rate > 30 (1 point), Systolic BP <90 mmHg (1 point), Age > 65 years (1 point)
- 1 point: Low risk of mortality (0–5%), 2 points: Moderate risk of mortality: 9%, 3–5 points: High risk of mortality (15–40%).

Appendix C

Reference Ranges for Selected Clinical Laboratory Tests

Substance	Fluid[a]	Traditional units	×	k	=	SI units
Acetoacetate	P, S	0.3–3.0 mg/dL		97.95		3–30 μmol/L
Alanine aminotransferase (ALT, SGPT)	S	7–41 U/L		0.016		0.12–0.70 μkat/L
Albumin	S	4.1–5.3 g/dL		10		41–53 g/L
Female albumin	S	4.0–5.0 g/L		10		40–50 g/L
Male albumin	S					
Albumin	CSF	11–48 mg/dL		0.01		0.11–0.48 g/L
Aldolase	S	1.5–8.1 U/L		17.33		26–138 nkat/L
Alkaline phosphate	S	(F) 30–100 U/L		0.016		0.5–1.92 μkat/L
		(M) 45–115 U/L				0.75–1.92 μkat/L
Alpha fetoprotein (adult)	S	0–8.5 ng/mL		1		0–8.5 μg/L
Ammonia, as NH_3	P	19–60 μg/dL		0.587		11–35 μmol/L
Amylase (method dependent)	S	20–96 U/L		0.016		0.34–1.6 μkat/L
Anion gap	S	7–16 mmol/L		1		7–16 mmol/L
Arterial blood gases						
$\left[\mathrm{HCO}_3^-\right]$		22–30 mEq/L		1		22–30 mmol/L
PCO_2		32–45 mmHg		0.134		4.3–6.0 kPa
pH		7.35–7.45		1		7.35–7.45
PO_2		72–104 mmHg		0.134		9.6–13.8 kPa
Aspartate aminotransferase (AST, SGOT)	S	12–38 U/L		0.016		0.20–0.65 μkat/L
B-type natriuretic peptide (BNP)	P	Age and gender specific: <167 pg/mL		1		Age and gender specific: <167 ng/L
Bilirubin	S					
Total (bilirubin)		0.3–1.3 mg/dL		17.1		5.1–22 μmol/L
Direct (bilirubin)		0.1–0.4 mg/dL		17.1		1.7–6.8 μmol/L
Indirect (bilirubin)		0.2–0.9 mg/dL		17.1		3.4–15.2 μmol/L
β-Hydroxybutyrate	S	<1.0 mg/dL		96.05		<100 μmol/L
Bicarbonate	S	22–26 mEq/L		1		22–26 mmol/L
Blood urea nitrogen (BUN)	P, S	8–18 mg/dL		0.367		3.0–6.5 mmol/L
Calcium-Total	S	8.7–10.2 mg/dL		0.252		2.2–2.6 mmol/L

(continued)

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Substance	Fluid[a]	Traditional units	×	k	=	SI units
Calcium ionized	WB	4.5–5.3 mg/dL		0.25		1.12–1.32 mmol/L
Carboxyhemoglobin (carbon monoxide content)	WB	>20%		0.01		>0.2 proportion of 1
Nonsmokers		0–4%		0.01		0–0.04
Smokers		4–9%		0.01		0.04–0.09
Onset of symptoms		15–20%		0.01		0.15–0.20
Loss of consciousness and death		>50%		0.01		>0.50
Chloride	S	102–109 mEq/L		1		102–109 mmol/L
	CSF	120–130 mEq/L		1		120–130 mmol/L
	U	10–200 mEq/L		1		10–200 mmol/L
Cholinesterase	S	5–12 U/mL		1		5–12 kU/L
Complement						
C3	S	83–177 mg/dL		0.01		0.83–1.77 g/L
C4	S	16–47 mg/dL		0.01		0.16–0.47 g/L
Cortisol: Fasting, 8 a.m.–12 noon, 12 noon–8 p.m., 8 p.m.–8 a.m.						
	S	5–25 µg/dL 5–15 µg/dL 0–10 µg/dL		27.588 27.588 27.588		138–690 nmol/L 138–414 nmol/L 0–276 nmol/L
Cortisol, free	U	20–70 µg/24 h		2.758		55–193 nmol/24 h
C-reactive protein	S	0.2–3.0 mg/L		1		0.2–3.0 mg/L
Creatine kinase (total): Female Males	S	39–238 U/L 51–294 U/L		0.017 0.017		0.66–4.0 µkat/L 0.87–5.0 µkat/L
Creatine kinase-MB	S					
Mass		0.0–5.5 ng/mL		1		0.0–5.5 g/L
Fraction of total activity (by electrophoresis)		0–4.0%		0.01		0–0.04
Creatinine: Female Male	S	0.5–0.9 ng/mL 0.6–1.2 ng/mL		88.4 88.4		44–80 µmol/L 53–106 µmol/L
Creatinine	U	15–25 mg/kg/24 h		0.009		0.13–0.22 mmol/kg/24 h
Cyanide: Nontoxic	WB	<µg/dL		3.8		<19 µmol/L
Cyanide: Lethal		>30 µg/dL				>114 µmol/L
Erythropoietin	S	4–27 U/L		1		4–27 U/L
Fatty acids, free (nonesterified)	P	<8–25 mg/dL		0.0355		<0.28–0.89 mmol/L
Ferritin Female Male	S	10–150 ng/dL 29–248 ng/mL		1 1		10–150 µg/dL 29–248 µg/L
Fibrinogen	P	150–350 mg/dL		0.01		1.5–3.5 g/L
Fibrin split products	S	<10 µg/mL		1		<10 mg/L
Glucose	P					
Glucose (fasting)	P	70–100 mg/dL		0.06		3.9–6.1 mmol/L
Glucose	CSF	50–80 mg/dL		0.06		2.8–4.4 mmol/L
Impaired glucose tolerance		111–125 mg/dL		0.056		6.2–6.9 mmol/L
Diabetes mellitus		>125 mg/dL		0.056		>7.0 mmol/L

(continued)

Substance	Fluid[a]	Traditional units	×	k	=	SI units
Glucose, 2 h postprandial	P	70–120 mg/dL		0.056		3.9–6.7 mmol/L
Hemoglobin (Hb)	P	0.6–5.0 mg/dL		10		6–50 mg/L
Adult males (Hb)	WB	13.3–16.2 g/dL		10		133–162 g/L
Adult females (Hb)	WB	12–15.8 g/dL		10		120–158 g/dL
Mean corpuscular hemoglobin (MCH)	WB	26–34 pg/cell		1		26–34 pg/cell
Mean corpuscular hemoglobin concentration (MCHC)	WB	33–37 g/dL		10		330–370 g/L
Mean corpuscular volume (MCV)	WB	80–100 µm^3		1		80–100 fL
Hemoglobin A_{lc}	WB	4.0–6.0%		0.01		0.04–0.06 Hb fraction
Homocysteine	P	4.4–10.8 µmol/L		1		4.4–10.8 µmol/L
Iron	S	41–141 µg/dL		0.178		7–25 µmol/L
Iron-binding capacity	S	251–406 µg/dL		0.179		45–73 µmol/L
Lactate	P, arterial	4.5–14.4 mg/dL		0.111		0.5–1.6 mmol/L
	P, venous	4.5–19.8 mg/dL		0.111		0.5–2.2 mmol/L
Lactate: Resting	P	<2.0 mEq/L		1		<2 mmol/L
Exercise		<4.0 mEq/L				<4 mmol/L
Lactate dehydrogenase	S	115–221 U/L		0.0171		2.0–3.8 µkat/L
Lipase	S	3–43 U/L		0.166		0.5–0.73 µkat/L
Magnesium	S	1.5–2.3 mg/dL		0.413		0.62–0.95 mmol/L
Methemoglobin	WB	0–1% of total Hb		0.01		0.0–0.01 proportion of total Hb
Microalbumin urine 24-h urine Spot urine	U	0–30 mg/24 h 0–30 µg/mg creatinine		0.001 0.001		0.0–0.03 g/day 0.0–0.03 g/g creatinine
Myoglobin Male Female	S	19–92 µg/L 12–76 µg/L		1 1		19–92 µg/L 12–76 µg/L
Osmolality	P	275–295 mOsm/kg serum water		1		275–295 mOsm/kg serum water
	U	500–800 mOsm/kg water		1		500–800 mOsm/kg water
Phosphatase, alkaline	S	33–96 U/L		0.0169		0.56–1.63 µkat/L
Phosphorus, inorganic	S	2.5–4.3 mg/dL		0.324		0.81–1.4 mmol/L
Potassium	S	3.5–5.0 mEq/L		1		3.5–5.0 mmol/L
Prealbumin	S	17–34 mg/dL		10		170–340 mg/L
Prolactin	S	0–20 ng/mL		1		0–20 g/L
Prostate-specific antigen (PSA) <40 years male >40 years male	S	0.0–2.0 ng/mL 0.0–0.40 ng/mL		1 1		0.0–2.0 µg/L 0.0–0.4 µg/L
PSA, free; in males 45–75 years, with PSA values between 4 and 20 g/mL	S	>25% associated with benign prostatic hyperplasia		0.01		>0.25% associated with benign prostatic hyperplasia
Protein fractions	S					
Albumin		3.5–5.5 g/dL (50–60%)		10		35–55 g/L

(continued)

Substance	Fluid[a]	Traditional units	×	k	=	SI units
Globulin		2.0–3.5 g/dL (40–50%)		10		20–35 g/L
Alpha$_1$		0.2–0.4 g/dL (4.2–7.2%)		10		2–4 g/L
Alpha$_2$		0.5–0.9 g/dL (6.8–12%)		10		5–9 g/L
Beta		0.6–1.1 g/dL (9.3–15%)		10		6–11 g/L
Gamma		0.7–1.7 g/dL (13–23%)		10		7–17 g/L
Total protein	P, S	6.0–8.0 g/dL/L		10		60–80 g/L
	CSF	<40 mg/dL		0.01		<0.40 g/L
	U	<150 mg/24 h		0.01		<1.5 g/24 h
Sodium	S	136–146 mEq/L		1		136–146 mmol/L
Thyroid-stimulating hormone	S	0.34–4.25 μIU/mL		1		0.34–4.25 mIU/L
Thyroxine, free (fT_4)	S	0.8–1.7 ng/dL		12.871		10.3–21.9 pmol/L
Thyroxine, total (T_4)	S	5.4–11.7 μg/dL		12.871		70–151 nmol/L
Triiodothyronine (T_3)	S	75–220 pg/dL		0.015		12–3.4 pmol/L
Troponin I Normal population, 99% tile Cutoff for MI	S	0–0.08 ng/mL >0.4 ng/mL		1 1		0–0.08 μg/L >0.4 μg/L
Troponin T Normal population, 99% tile Cutoff for MI	S	0–0.01 ng/mL 0–0.1 ng/mL		0.1 1		0–0.1 μg/L 0–0.1 μg/L
Urea nitrogen	S	7–20 mg/dL		0.357		2.5–7.1 mmol/L
Uric acid Females Males	S	2.5–5.6 mg/dL 3.1–7.0 mg/dL		0.06 0.06		0.15–0.33 μmol/L 0.18–0.41 μmol/L
Urobilinogen	U	1–3.5 mg/24 h		1.7		1.7–5.9 μmol/d

Adapted from the New England Journal of Medicine SI Unit Conversion Guide. Waltham, MA: Massachusetts Medical Society, 1992

[a] *P* plasma, *S* serum, *U* urine, *WB* whole blood, *CSF* cerebrospinal fluid, *RBC* red blood cell

Reference ranges for vitamins and trace elements

Substance	Fluid[a]	Traditional units	×	k	=	SI units
Chromium	S	0.14–0.15 ng/mL		17.85		2.5–2.7 nmol/L
Copper	S	70–140 μg/dL		0.16		11–22 μmol/L
Folate	RBC	140–960 ng/mL		2.26		317–2196 nmol/L
Iron	S	(M) 80–180 μg/dL		0.18		(M) 14–32 μmol/L
		(F) 60–160 μg/dL				(F) 11–29 μmol/L
Ferritin	P, S	(M) 20–250 ng/mL		1		(M) 20–250 μg/L
		(F) 10–120 ng/mL				(F) 10–120 μg/L
Manganese	WB	0.4–2.0 μg/dL		0.018		0.7–3.6 μmol/L
Pyridoxine	P	20–90 ng/mL		5.98		120–540 nmol/L
Riboflavin	S	2.6–3.7 μg/dL		26.57		70–100 nmol/L
Selenium	WB	58–234 μg/dL		0.012		0.7–2.5 μmol/L

(continued)

Substance	Fluid[a]	Traditional units	×	k	=	SI units
Thiamine (total)	P	3.4–4.8 µg/dL		0.003		98.6–139 µmol/L
Vitamin A	P, S	10–50 µg/dL		0.349		0.35–1.75 µmol/L
Vitamin B_{12}	S	200–1000 pg/mL		0.737		150–750 pmol/L
Vitamin C	S	0.6–2 mg/dL		56.78		30–100 µmol/L
Vitamin D	S	24–40 ng/mL		2.599		60–105 nmol/L
Vitamin E	P, S	0.78–1.25 mg/dL		23.22		18–29 µmol/L
Zinc	S	70–120 µg/dL		0.153		11.5–18.5 µmol/L

Adapted from the New England Journal of Medicine SI Unit Conversion Guide. Waltham, MA: Massachusetts Medical Society, 1992

[a] *P* plasma, *S* serum, *U* urine, *WB* whole blood, *CSF* cerebrospinal fluid, *RBC* red blood cell

Appendix D: Syllabus for ICU Training

Narendra Rungta and Arvind Kumar Baronia

I. **Domains**
  1. Resuscitation
  2. Disease Management: Diagnosis/Monitoring/Supportive care
  3. Procedure
  4. Perioperative Care
  5. Transport
  6. Ethics/End of Life Care/Prognostication
  7. Quality and Patient Safety
  8. Administration/Clinical Governance
  9. Research/Teaching
  10. Professionalism/Communication
  11. Medico Legal
  12. Organ donation

II. Competencies
  1. Resuscitaion
    (a) Assess and stabilize patients with Shock/Respiratory failure/other organ failure
    (b) Assess and stabilize patient with acute physiologic derangement
    (c) Assess and stabilize patients with Shock/Respiratory failure/other organ failure
    (d) Assess and stabilize patient with acute physiologic derangement/Rapid response
    (e) Manage Cardiorespiratory arrest and post arrest care
    (f) Manage Trauma/Burn/Environmental hazards
    (g) Disaster management and Mass casualty Management
    (h) Triaging
    (i) Resuscitation in special situations: Obstetrics/Pediatric

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2. Disease Management: Diagnosis/Monitoring/Supportive care/Definitive care
    (a) History taking
    (b) Focused physical examination
    (c) Relevant investigation/imaging
    (d) Provisional and Differential diagnosis
    (e) Interdepartment consultation
    (f) Documentation
    (g) General monitoring
    (h) Organ-specific monitoring
    (i) Hemodynamic support
    (j) Respiratory support
    (k) Renal support
    (l) Nutritional support
    (m) Neurological support
    (n) Hematological support
    (o) Metabolic support
    (p) Immunological support
    (q) Physiotherapy
    (r) Definitive care
3. Procedures
    (a) Organ specific procedures
4. Perioperative care
    Competencies
    (a) Perioperative care of high-risk surgical patient
    (b) Perioperative care in cardiac surgery
    (c) Perioperative care in neurosurgery
    (d) Perioperative care in Transplant surgery
    (e) Perioperative care in Thoracic surgery
    (f) Perioperative care in Trauma surgery
5. Transport
    (a) Intrahospital transport of high-risk patient
    (b) Interhospital Ground/Air Transport of High risk patient
    (c) Transport of patient with contagious disease
    (d) Documentation/Hand over
6. Ethics/End of Life/Prognostication
    (a) Prognostication Scoring systems
    (b) Withholding and Withdrawing life support: Communication
    (c) Principles of medical ethics
    (d) Palliative care
    (e) Empathy towards Family and Religious belief
7. Quality and Patient safety
    (a) Structure, Process and Outcome data on Quality
    (b) Root Cause analysis of Near Miss and Medical errors
    (c) Medication safety and Adverse drug reaction monitoring

    (d) Auditing and Benchmarking performance
    (e) Environmental hazards and safety of patient and health care staff
    (f) Infection control measures

8. Administration/Clinical Governance
    (a) Human Resource/Design/Equipment/Budgeting
    (b) Conflict resolution
    (c) Team leader role
    (d) Critical Care Outreach team
    (e) Critical care follow up clinic
    (f) Admission and discharge planning
    (g) Developing ICU policies and Protocols
9. Research/Teaching
    (a) Plan Research Project
    (b) GCP training
    (c) Critically appraising a research paper
    (d) Participate in departments teaching/research programs
    (e) Simulation training
    (f) Teaching Nurse/Allied health care Professional
    (g) Presentation in Scientific meetings
10. Professionalism
    (a) Professional attitude/communication towards patients, family, colleagues
    (b) Patient care related documents
    (c) Respects privacy, confidentiality of patients data
    (d) Involves patient and family in decision making
    (e) Promotes team management and multidisciplinary care
    (f) Patient and Family centered care
    (g) Understand principles of reducing cost while maintaining quality
11. Medico legal
    (a) State and National laws
    (b) Medical negligence
    (c) Informed consent
    (d) Medical indemnity
12. Organ Donation:
    (a) Certifying Brain Death
    (b) Managing Organ donor/Organ Transport

III. Aggregated Syllabus

1. General
    (a) ICU infrastructure: building, equipment and manpower
    (b) Organization of critical care services: models of intensive care and outreach services
    (c) Critical care physiology (system-wise)

    (d) Assessment of critically ill patients
    (e) Monitoring in the ICU
    (f) Principles of critical care pharmacology, Drug interactions and toxicity, Pharmacology of sedatives, hypnotic agents, analgesics, and neuromuscular blocking agents
    (g) Pain management
    (h) Scoring system in the ICU
    (i) Enteral and parenteral nutrition
    (j) Care of ICU equipment-electrical safety, calibration, decontamination, and maintenance
    (k) Intra- and inter-hospital transport of critically ill patients
    (l) Basics of imaging modalities including ultrasound, X-ray, CT, MRI, and Angiography in the ICU patients
    (m) Systemic disorders in critical illness
    (n) Obesity-hypoventilation syndrome and obstructive sleep apnea syndrome

2. Fluid and electrolytes
    (a) Fluid requirements in critically ill patients
    (b) Monitoring of fluid therapy and diagnosis of inappropriate fluid therapy, i.e., fluid overload and hypovolemia
    (c) Colloid versus crystalloid
    (d) Electrolyte disturbances (calcium, magnesium, potassium, sodium, and phosphorus) in ICU
    (e) Hyperosmolar therapies—Hypertonic saline
    (f) Acid-base disorders—Bicarbonate and Anion Gap, Base Deficit, Stewart approach
    (g) Fluid therapy in children
3. Renal disorders
    (a) Acute kidney injury
    (b) Renal tubular acidosis
    (c) Hepatorenal syndrome
    (d) Peritoneal dialysis, plasmapheresis, and apheresis
    (e) Renal replacement therapy
    (f) Drugs in renal failure
4. Nervous system
    (a) Seizure disorders and status epileptics
    (b) Cerebrovascular accident (CVA)
    (c) Acute CNS infections
    (d) Intra-arterial pressure: Physiology, Intracranial hypertension, ICP monitoring
    (e) Coma
    (f) Traumatic brain injury
    (g) Neuromuscular diseases
    (h) Acute Flaccid Paralysis-Guillain-Barré syndrome and other disorders
    (i) Tetanus
    (j) CNS drugs

   - (k) Brain death
   - (l) EEG in the ICU
5. Cardiovascular system
   - (a) Acute coronary syndrome
   - (b) Acute heart failure
   - (c) ACLS guidelines
   - (d) Rhythm disorders
   - (e) Basics of echocardiography in the ICU
   - (f) Valvular heart diseases
   - (g) Cardiomyopathies
   - (h) Postoperative cardiac care
   - (i) Cardiogenic shock
   - (j) Myocarditis
   - (k) Hypertensive emergencies
   - (l) Cardioversion
   - (m) Cardiac drugs
6. Environmental disorders
   - (a) Near-drowning
   - (b) Thermal injuries
   - (c) Biochemical hazards
   - (d) Radiation hazards
   - (e) Polytrauma
   - (f) Disaster management guidelines
   - (g) Envenomation
   - (h) Acute poisoning
7. Endocrinal disorders
   - (a) Thyroid storm and other thyroid disorder in critical care
   - (b) Diabetic ketoacidosis (DKA)
   - (c) Adrenal insufficiency
   - (d) Cerebral salt wasting
   - (e) Hyperglycemia and hypoglycemia in the ICU
8. Gastrointestinal disorders
   - (a) Upper gastrointestinal bleeding
   - (b) Lower gastrointestinal bleeding
   - (c) Acute liver failure
   - (d) Acute pancreatitis
   - (e) Acute abdomen-medical and surgical emergencies
   - (f) Stress ulcer prophylaxis
   - (g) Postoperative care
   - (h) Liver transplant: Basics
9. Respiratory disorders
   - (a) Oxygen therapy
   - (b) Airway adjuncts
   - (c) Basics of mechanical ventilation and applied physiology
   - (d) Disease-specific ventilation

   (e) Ventilator-Graphics, monitoring, and Troubleshooting
   (f) High-frequency oscillation ventilation
   (g) Acute respiratory distress syndrome
   (h) Pulmonary thromboembolism
   (i) Pneumonias
   (j) Chronic obstructive pulmonary disease
   (k) Noninvasive ventilation
   (l) Chest physiotherapy
   (m) Pulmonary function test (PFT)
   (n) Extracorporeal membrane oxygenation (ECMO) + ECCO$_2$ Elimination: asics

10. Infections
    (a) Hand hygiene
    (b) Asepsis guidelines
    (c) Sepsis syndrome: SIRS, sepsis, severe sepsis, septic shock and multiorgan dysfunction syndrome (MODS)
    (d) Immunocompromised hosts
    (e) HIV and AIDS
    (f) Ventilator-associated pneumonia (VAP)
    (g) New outset fever in the ICU
    (h) Severe Tropical infections: Malaria, Typhoid, Scrub typhus, and zoonosis
    (i) Nosocomial infections
    (j) Viral hemorrhagic fevers
    (k) Endocarditis
    (l) Opportunistic infections in the ICU
    (m) Fungal infections
    (n) Infection control measures in the ICU
    (o) Antimicrobial therapy
    (p) Prevention of Antibiotic Resistance in the ICU
    (q) Antibiotic resistance and MDR pathogens
11. Obstetric disorders
    (a) Pregnancy-induced hypertension
    (b) Acute hemorrhage
    (c) Trauma in pregnancy
    (d) HELPP syndrome
    (e) Cardiomyopathy in pregnancy
    (f) Amniotic fluid embolism
12. Procedures
    (a) Endotracheal Intubation
    (b) Percutaneous tracheostomy
    (c) Flexible bronchoscopy
    (d) Intercostal drainage
    (e) Intracranial pressure monitoring
    (f) EEG interpretation
    (g) Peritoneal dialysis

   (h) Continuous renal replacement therapy
   (i) Cardiac pacing
   (j) ECG
   (k) CPR
   (l) Defibrillation
   (m) Pericardiocentesis
   (n) Central venous access
   (o) Echo cardiography (ECHO)
   (p) Emergency ultrasonography
   (q) Emergency radiology
   (r) Percutaneous endoscopic gastrostomy (PEG)
   (s) Intra-abdominal pressure monitoring
13. Hematology
   (a) Blood component therapy
   (b) Thrombocytopenia in the ICU
   (c) Oncology-related life-threatening issues in critical care
   (d) Laboratory tests: Interpretation
14. Research
   (a) Basics-statistical definitions
   (b) Sample size calculations, study designs, data collection
   (c) Generation of research ideas and hypotheses
   (d) Interpretation of results
   (e) Understanding evidence-based medicine in critical care
15. Miscellaneous
   (a) Do not attempt resuscitation (DNAR)
   (b) Medical ethics
   (c) Withholding and withdrawing care
   (d) Organ donation
   (e) Legal issues—Laws related to ICU
   (f) Anxiety and stress management in health care providers in ICU
   (g) Communication skills in acute care
   (h) Critical Care nursing-education
   (i) Quality care in the ICU-Bench marking
16. Skills
   (a) Endotracheal intubation
   (b) Difficult airway management
   (c) Flexible bronchoscopy
   (d) Surgical airway
   (e) Percutaneous tracheostomy
   (f) Needle thoracotomy
   (g) Chest tube insertion
   (h) Initiation of ventilation
   (i) Care of equipment
   (j) Central venous access
   (k) Intra-arterial pressure monitoring

(l) Defibrillation
(m) Pacing
(n) Cardiac output measurement
(o) Gastric tonometry
(p) Peritoneal dialysis
(q) Continuous renal replacement therapy
(r) Intra-abdominal pressure monitoring
(s) Interpretation of ECG/arterial blood gas/Ventilator waveforms
(t) Chest physiotherapy
(u) Lumbar puncture
(v) Intracranial pressure monitoring
(w) Intraosseous insertion

Glossary of Statistical Terms

Absolute Risk Reduction (Risk difference) The difference in mortality in treatment and control arm.

Accuracy Number of true positives and true negatives divided by the total number of observations.

Analysis of Variance (ANOVA) Method of comparing means of two or more samples to see whether they come from the same population.

Association Describes relationship between two variables.

Attributable Risk It is calculated by subtracting the incidence of a disease in nonexposed persons from the incidence of disease in exposed persons.

Bayesian Statistics An alternative way of analyzing data by combining numerical values for prior belief, existing data, and new data.

Bimodal distribution When there are two modes in a set of data.

Binomial distribution If the data can take only one of two values, e.g., male or female.

Case-control study A case-control study starts with the outcome of interest and works backward to the exposure. For instance, patients with a disease are identified and compared with controls for exposure to a risk factor. In this model, relative risk or the incidence of disease cannot be calculated. However, in case-control studies, the odds ratio provides a reasonable estimate of the relative risk.

Categorical Variables Representing different categories of the same feature, e.g., different blood group, different eye colors, etc. When there is an inherent order in the variables like mild, moderate, or severe, it is called "ordinal" variable.

Chi Square Test Test of association between two categorical variables.

Cohort study A cohort study is a particular form of longitudinal study that samples a cohort (a group of people who share a defining characteristic, typically those who experienced a common event in a selected period, such as birth or graduation), performing a cross-section at intervals through time.

Confidence interval The boundaries of a confidence interval give values within which there is a high probability (95% by convention) that the true population value can be found. The calculation of a confidence interval considers the standard deviation of the data and the number of observations. Thus, a confidence interval narrows as the number of observations increases, or its variance (dispersion) decreases.

Confounding Effect of a factor that cannot be separated out in an experiment.

Continuous variable A variable which can take any value within a given range.

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Correlation When there is a linear relationship between two variables. Measured on a scale of −1 (perfect negative correlation), 0 (no correlation) to +1 (perfect positive correlation).

Correlation Coefficient Measure of strength of the linear relationship between two variables.

Cox proportional hazards analysis Cox proportional hazards analysis is similar to logistic regression because it can account for many variables that are relevant for predicting a dichotomous outcome. However, logistic regression analysis, Cox proportional hazards analysis permits time to be included as a variable, and for patients to be counted only for the period of time in which they were observed.

Cox regression Model A method which explores the effect of different variables on survival.

Descriptive statistics Values which describe the data in a sample.

Discrete variable The data can only be of certain values, e.g., number of children in a family.

Fishers Exact Test Test for association between categorical variables.

Histogram A graph of continuous data categorized in a number of classes.

Incidence Number of new events that have occurred in a specific time interval divided by the population at risk at the beginning of the time interval. The result gives the likelihood of developing an event in that time.

Intention to treat The central principle underlying intention-to-treat analysis is that study participants should be analyzed according to the groups in which they were randomized, even if they did not receive or comply with treatment. Such analysis is contrasted to "as treated" (or "per protocol") analysis in which subjects are analyzed according to the actual treatment they received.

Intention to treat Analysis according to the group in which the patient were randomized even if they are withdrawn from the study or did not receive the treatment or crossed over.

Interquartile range The upper and lower values defining the central 50% of observations. The boundaries are equal to the observations representing the 25th and 75th percentiles. The interquartile range is depicted in a box and whiskers plot.

Kaplan-Meier analysis Kaplan-Meier analysis measures the ratio of surviving patients (or those free from an outcome) divided by the total number of patients at risk for the outcome. Every time a patient has an outcome, the ratio is recalculated. Using these calculations, a curve can be generated that graphically depicts the probability of survival as time passes.

Kappa Level of agreement between two categorical measures.

Kruskal–Wallis test Non-parametric test which compares two or more independent groups.

Likelihood Ratio Likelihood ratios are an expression of sensitivity and specificity that can be used to estimate the odds that a condition is present or absent.

Log rank Test A non-parametric test used for the comparison of survival estimates.

Logistic regression analysis Models in which the outcome is dichotomous (e.g., alive or dead, or a complication occurs or does not occur).

Mann–Whitney U test A non-parametric test to see whether there is a significant difference between two sets of data that has come from two different set of subject.

Mean Sum of observations divided by the number of observations.

Median Observation in the middle, when all observations are ranked from smallest to largest; when number of observations are even, the median is defined as the mean of the middle two data points.

Mode Observation which occurs most frequently.

Multivariate analysis (Regression analysis) Statistical methods that can simultaneously account for multiple variables are known as "multivariate" (or multivariable) analysis. These methods help to "control" (or "adjust") for variables that are extraneous to the main causal question and might confound it.

Negative likelihood ratio It is calculated by dividing 1 minus sensitivity by specificity (1 − sensitivity)/specificity). Positive and negative likelihood ratios of 9 and 0.25, for example, can be interpreted as meaning that a positive result is seen 9 times as frequently while a negative test is seen 0.25 times as frequently in those with a specific condition than those without it.

Negative predictive value It represents the likelihood that a patient who has a negative test is free of disease. The predictive value depends upon the prevalence of a disease within a population.

Nominal Data Data that can be placed in a particular category but have no particular order.

Non Parametric test A test which is not dependent on distribution of data.

Normal distribution Distribution of data that is symmetrical and have a bell-shaped curve.

Null hypothesis The null hypothesis is the theory that the exposure or intervention that is being studied is not associated with the outcome of interest. Thus, if a certain level of statistical significance is reached, the null hypothesis will be rejected, otherwise the null hypothesis will not be rejected.

Number needed to Harm (NNH) The absolute side effects rate for placebo minus the absolute side effect for treated patients.

Number needed to treat (NNT) NNT is the reciprocal of the absolute risk reduction (the absolute adverse event rate for placebo minus the absolute adverse event rate for treated patients): 1/ARR.

Odds ratio Odds that an individual with a specific condition has been exposed to a risk factor divided by the odds that an individual without that condition (control) has been exposed. The odds ratio is used in case-control studies and is also used in multivariate analyses. The relative risk and odds ratio are interpreted relative to the number one.

One tailed Test A test where the null hypothesis can only be rejected in one direction (better or worse).

Ordinal data Data that can allocated to categories in an ordered manner, e.g., stages of malignancy.

Parametric test Any test that assumes that the data needs to follow a certain distribution, e.g., normal distribution.

Pearson Correlation coefficient Calculating correlation coefficient if values are sampled from a normal population.

Percentile Percentage of a distribution that is below a specific value. As an example, a child is in 90th percentile for weight if only 10% of children of the same age weigh more than she/he does.

Period prevalence Proportion of individuals with a condition during a specified interval (e.g., a year).

Person-years Total number of years that each member of a study population has been under observation or treatment. Multiplying the number of years by the number of members of a sample population studied.

Point prevalence Proportion of individuals with a condition at a specified point in time.

Poisson distribution Number of events occurring in a fixed time interval, e.g., number of deaths in a year.

Positive likelihood ratio It is calculated by dividing sensitivity by 1 minus specificity (sensitivity/(1 − specificity)).

Positive Predictive Value Likelihood that a patient with a positive test has the disease.

Prevalence Number of individuals with a given disease at a given point in time divided by the population at risk at that point in time. Prevalence has been further defined as being "point" or "period."

P-Value A p-value is a measure of the effect of chance within a study. It is not the probability that the result of the study is true or correct. Instead, it is the probability that if the null hypothesis were true, and if the results were not affected by bias or confounding, that we would have seen a result as extreme or more extreme than the one seen in the study.

Randomized controlled trial A randomized controlled trial (RCT) is an experimental design in which patients are assigned to two or more interventions. One group of patients is often assigned to a placebo (placebo control) but a randomized trial can involve two active therapies (active control).

Range Difference between the largest and smallest observation.

Receiver Operating Curve (ROC) curve It plots sensitivity on the Y axis, and 1-specificity (which is the false positive rate) on the X axis.

Regression Finding a relationship between two variables where one is dependent on the other.

Relative risk (or risk ratio) Incidence in exposed individuals divided by the incidence in unexposed individuals. This is used in cohort study.

Sensitivity The number of patients with a positive test who have a disease divided by all patients who have the disease. A test with high sensitivity will not miss many patients who have the disease (i.e., few false negative results).

Spearman correlation coefficient An estimate of correlation used for nonparametric variables.

Specificity The number of patients who have a negative test and do not have the disease divided by the number of patients who do not have the disease.

Standard Deviation Variability of data around the mean. In "normal" distribution samples (i.e., Gaussian), 68 and 95% of values fall within one and two standard deviations of the mean, respectively.

Standard Error of the Mean It describes how much variability can be expected when measuring the mean from several different samples.

t-test (Student t-test) It is a parametric test used to compare means of two groups.

Two Tailed test A test where the null hypothesis can be rejected whether the treatment is better or worse.

Type I Error (also referred to as an "alpha error") It is incorrectly concluding that there is a statistically significant difference in a dataset when it is not present; the probability of making a type I error is called "alpha." A typical value for alpha is 0.05. Thus, a $p < 0.05$ leads to a decision to reject the null hypothesis.

Type II error (also referred to as a "beta error") It is incorrectly concluding that there was no statistically significant difference in a dataset and when actually it is present; the probability of making a type II error is called "beta." This error often reflects insufficient power of the study.

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